FRONTOSTRIATAL CIRCUITS AND SELECTION OF TASK-RELEVANT INFORMATION

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“I could have done thousands
of different things, but
I would have thought
thousands of different times
to do what I am doing now…”

-CC-

…To my family…

Summary

Abstract

The main aim of this research project was to investigate the function of the prefrontal cortex and basal ganglia of selection of task-relevant information. To that purpose, different tasks and methodologies were used in the domain of the higher levels of the language production system.

The first part of the thesis concerns with dynamic aphasia. This is a sever impairment in propositional language production characterized by an exceptionally reduced spontaneous speech in the context of well-preserved naming, articulation, prosody and repetition skills. It has been proposed that the ability to select responses from among alternative options can be dramatically reduced in this syndrome. Most of the documented cases of dynamic aphasia have been described following lesions occurring to left frontal regions. However, a few cases of dynamic aphasics following lesion to basal ganglia have been reported. The patient that we studied represents one of these rare cases. In line with previous evidence we found that our patient was particularly impaired in selecting verbal responses from among competing options, thus suggesting that basal ganglia contribute to the process of response selection and inhibition in domain other than motor behaviour. The patient also had problems in non-verbal domains suggesting the presence of a more general deficit of novel thought generation.

The results of the single case analysis motivated us to investigate the ability of selecting responses from among alternative options in normal adult subjects. A couple of behavioral studies showed that selecting a response from among others in competition takes longer than selecting a response which is more uniquely related with a stimulus. High selection demands conditions were also shown to be more prone to dual-task interference than conditions with low selection demands.

Moreover we have modeled dynamic aphasia using the COGENT information-processing package. A computational model, focused on a sentence completion task, implemented some of the higher-level processes of language production and successfully reproduced patient's difficulties on this task. The model has suggested that the language output disorder of our dynamic aphasic patient may be due to a decreased activation of verbal responses within a contention scheduling framework.

In the second part of the thesis we have further investigated the role of fronto-striatal circuits in the selection of task-relevant verbal information. We used a paradigm of noun and verb generation which allowed us to dissociate the roles that different factors, such as selection of responses from among alternative options and strength of stimulus-response association, play in single word generation. We carried out three studies on this topic. In the first of these, patients with Parkinson’s disease and normal older controls were asked to generate nouns and verbs from noun-stimuli which differed in selection demands (high and low) and association strength (weak and strong). PD patients had the greatest difficulties with the weakly stimulus-related verbs. Their poor performance was in part due to task-irrelevant responses which interfered during verb generation.

A unitary account of performance in word generation, based on the functional interaction between aspects of response selection and stimulus-response association strength, was proposed. A cognitive model that relied on basic models of associative retrieval (ACT-R memory theory) and on general theories of executive control was developed in order to reproduce the performance of young adults, older adults, and PD patients on the noun and verb generation tasks. Simulation results showed that PD patients and older controls differ particularly in the ability to inhibit task-irrelevant responses and in the speed of release from a retrieval failure.

Finally we also carried out an fMRI study on adult subjects using the same noun and verb generation tasks. The results highlight a functional segregation within the left inferior frontal gyrus, particularly for verb generation. The anterior/ventral section of this brain region is involved in controlled retrieval from semantic memory whereas the mid/posterior section is more involved in post-retrieval selection in situations of high competition. Finally, the basal ganglia were more active when weakly associated verbs had to be produced relative to weakly associated nouns; thus additional activation of these subcortical structures was triggered particularly when task-irrelevant stimuli interfere with the current task (e.g. nouns during verb production).

Overall, the present project represents an instantiation of the fractionation approach recently adopted to study the supervisory functions of the prefrontal cortex and basal ganglia. This approach was used here in order to understand the role of these brain regions in the process of selection of task-relevant responses. A variety of approaches was used (i.e. functional neuroimaging, cognitive neuropsychology, and cognitive modelling) to pursuit our aims. Critically we have shown that the development of well specified models of normal cognition allows linking findings from functional neuroimaging and cognitive neuropsychology.

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Some of the experiments reported in the thesis have also been submitted elsewhere. Specifically, the single case analysis has been presented in an article recently published in *Neurocase* [Authors: Crescentini, C., Lunardelli, A., Mussoni, A., Zadini, A., & Shallice, T. (2008), *Neurocase, 14,* 184-203]; the COGENT computational model has been published two years ago in the *Proceedings of the Seventh International Conference on Cognitive Modelling* [Crescentini, C., Shallice, T., & Cooper, R., (2006), In D., Fum, F., Del Missier, F., & A., Stocco (Eds.), *Proceedings of the Seventh International Conference on Cognitive Modelling (ICCM-06).* Trieste, Italy: Edizioni Goliardiche, 88-93]; experiment presented in chapter 4 appeared this year on *Neuropsychologia* [Crescentini, C., Mondolo, F., Biasutti, E., & Shallice, T. (2008), *Neuropsychologia, 46,* 434-447]; the FRI model is part of a manuscript currently under revision for resubmission to *Psychonomic Bulletin and Review* [Crescentini, C., & Del Missier, F.]; the fMRI experiment is part of a paper which was resubmitted after a first revision to *The Journal of Cognitive Neuroscience* [Crescentini, C., Macaluso, E., & Shallice, T.].

Chapter 1

1.1. Methods of Cognitive Neuroscience

This thesis investigates the ability to select task-relevant information. The human ability to selectively adapt behaviour to different situations is a crucial requirement in our daily life. Our environment affords different behavioural options, only some of which are adaptive in any given situation. Therefore, we are very often required to select the contextual information that determines appropriate goal-oriented behavior. This control process is generally referred to as the selection of task-relevant information (Gazzaniga, Ivry, & Mangun, 2002). Cognitive neuroscience is making significant progress toward an understanding of such an ability.

The aims of cognitive neuroscience are fundamentally twofold. From the “cognitive” point of view, researchers in this field try to uncover and identify the elementary processes that may contribute to the overt behaviour (e.g. Gazzaniga et al., 2002). From the “neuroscientific” point of view, the aim of cognitive neuroscience is to find the neural mechanisms that underlie these processes. Importantly, as it will be shown in this thesis, the two aims are strictly interrelated and they can benefit from each other (e.g. Shallice, 1988).

Cognitive neuroscientists have used a number of different methods to understand the neural basis of human cognitive functions (e.g. Ellis & Young, 1988; Gazzaniga et al., 2002). Well-known techniques are the lesion method and the functional magnetic resonance imaging (fMRI) method. The lesion approach to structure/function relations dates back several centuries but was brought to our attention in particular in the 1800s by Broca and by the patient Phineas Gage (Harlow, 1848; Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994), who showed dramatic changes in cognitive and emotional behavior following an injury to the frontal cortex. Cognitive neuropsychology places particularly emphasis on the lesion method. It rests on the assumption that by studying people with selective disorders of cognition we can make inferences about the nature and the structure of cognitive functions (Shallice, 1988). Cognitive neuropsychology has in fact two main aims (Ellis & Young, 1988; Harley, 2004): 1) to explain the patterns of intact and impaired performance, observed in people with brain damage, in terms of impairment to one or more components of a model of normal cognitive functioning, and 2) to infer about normal cognitive processes from the patterns of performance shown by people with brain damage.

fMRI tells us more about brain functions. It relies on the paramagnetic properties of oxygenated and deoxygenated hemoglobin in order to get images of changing blood flow in the brain which are associated with neural activity. This allows the generation of images that reflect which brain structures are activated during performance of different cognitive tasks (Friston, Ashburner, Kiebel, Nichols, & Penny, 2007). Despite the criticisms which have frequently been risen to fMRI (e.g. Page, 2006, see below), this technique has widely been using for the last two decades. This is due to some advantages that fMRI inherently shows. For instance, it can non-invasively record brain signals without risks of radiation (present, for instance in CT scans), and it can record on a spatial resolution in the region of few millimetres even though it has relatively poor temporal resolution (in the order of seconds).

An important method used in cognitive neuroscience is computational modelling (McClelland, 1989; Anderson et al., 2004). Such a method has been employed to test theories of neuropsychological findings and to derive principles regarding brain-behavior relationships, but, as other methods, it has not been exempt from critiques. Computational modelling of cognitive processes (henceforth cognitive modelling) originated from Artificial Intelligence in the 1960s and has the aim to simulate or predict human behaviour through abstract representations of cognitive processes. This means that elements in a cognitive model correspond to elements of the hypothesized processes. There are several approaches to cognitive modelling (see next section) mainly differing in their assumptions about mental representation and in the way in which a cognitive model is put into a relation with the brain. Generally speaking, important features of a cognitive model are *completeness* and *faithfulness* (Cooper, 2002), namely, models should not neglect important aspects that may influence behavior (*completeness*), and they should not include component properties that are not likely to influence behavior (*faithfulness*). A productive way to study the characteristics of a model of a particular cognitive process is that provided by the *simulation* procedure. Simulation allows understanding how the component processes of a model operate and interact over a certain amount of time.

Contrasting ideas exist, among cognitive neuroscientists, on whether and how, neuropsychology findings, brain imaging findings, and results of simulations can be helpfully related to improve knowledge about brain-behavior relationship. Generally speaking, it has been proposed that cognitive modelling may play a key role in bridging “the gap between mind and brain” (Harley, 2004, p. 12; see also Anderson et al., 2004). Thus, simulation has been considered to provide a crucial contribution to the process of evaluation and exploration of cognitive processing theories (Cooper, 2002). Cognitive theories can in fact sometimes be very complex, consisting of many sub-processes that interact (Shallice, 1988; Ellis & Young, 1988); cognitive modelling helps to tease apart such sub-processes making explicit representational and processing assumptions about them. In this view cognitive modelling may represent a supplement to cognitive neuropsychology since, for instance, once a model of normal cognitive functioning is developed in a specific cognitive domain (e.g. reading), it can be “lesioned” in a pre-specified way, and its performance can be compared with that of patients with cognitive impairments (e.g. patients with dyslexia or alexia, Cooper, 2002; see also Plaut, McClelland, Seidenberg, & Patterson, 1996). Nonetheless, the relation between cognitive modelling and cognitive neuropsychology can be bidirectional as long as the latter informs the former by providing data against which models can be developed and tested. Despite the potential advantages of cognitive modelling, the usefulness of this method for understanding brain-behavior relationship has, however, been questioned. The first critique concerns the problems that may originate when models try to make detailed assumptions, for instance about processing and representation types, that do not rest on well-established empirical knowledge. For instance, a computational model of memory for lists of words may need to incorporate a process of memory decay. However, one has to specify details of the process and may have to decide between say a probabilistic process (i.e. words may spontaneously disappear from memory) and a process whereby memory representations vary in their strength, with decay affecting strength. Whatever is the choice one has to either specify the function which governs the probability of a word decaying at any specific moment or specify how strength changes with time. In this situation, many of those who criticize cognitive modelling may argue that insufficient evidence is available to decide on the correct decay process and thus tend to refuse models that include specifications that do not rest on purely empirical grounds. In a similar way, cognitive models have also been considered to be too powerful and, on the other hand, difficult to falsify (Harley, 2004; but see Cooper, 2002).

Findings from neuroimaging studies and findings from cognitive models have been related only in a few cases. The difficulty to specify, both anatomically and functionally, the processes that, in connectionist models, intervene between input (stimulus) and output (response) (i.e. hidden units, see next section), may be the reason why there has been little attempt to relate fMRI evidence to such models (Shallice, 2003). However, some exceptions exist; in an fMRI study of verbal short-term memory (VSTM), Henson, Burgess, and Frith (2000) have tried to localize in the brain the functions of 1) recoding, 2) storage, 3) rehearsal, and 4) temporal grouping. An existing connectionist model of VSTM (Burgess & Hitch, 1999) that makes explicit assumptions about the representation of temporal order was considered in order to explain the function of rehearsal. Henson et al. (2000) proposed a mapping of Burgess and Hitch's model onto different brain areas claiming that one specific area (left dorsolateral premotor cortex) was particularly important for the function of rehearsal.

Many more attempts have been made to use fMRI to test computational models derived from cognitive architectures (Anderson et al. 2004, see next section). As an example, Stocco and Anderson (2008) investigated the way in which prefrontal cortex and anterior cingulate cortex interact during performance on the symbolic paradigm of algebraic problem solving. The authors used ACT-R as the cognitive architecture (Anderson & Lebiere, 1998; Anderson et al., 2004) and found that their computational model was able to reproduce the time course of the BOLD signal which was observed in many task-related brain areas. These authors also mapped the different modules implemented in ACT-R to the brain areas that showed activation during execution of the algebraic task (see also Qin, Bothell, & Anderson, 2007, for further evidence on the relationship between fMRI and ACT-R).

Finally, the issue about how findings from cognitive neuropsychology and brain imaging can be related has not been less controversial than the issues concerning cognitive modelling. The debate has focused particularly on the usefulness of functional neuroimaging as a method for testing different psychological theories, and more generally, for learning more about cognition. Thus, both pessimistic (Poeppel, 1996; Uttal, 2001; see also Coltheart, 2006), and optimistic opinions (Shallice, 2003; 2004, Cappa, 2006; Jack, Sylvester, & Corbetta, 2006) have been given. Among the optimistic views, Henson (2005) has claimed that fMRI can be used as other dependent variables to tease apart different psychological theories as long as we assume the existence of a mapping from psychological function to brain structure. In this view it has been argued that fMRI can be applied to test theories of, for instance, visual attention (Downing, Liu, & Kanwisher, 2001), problem solving (Anderson et al., sumitted), and memory retrieval (Donaldson, Petersen, & Buckner, 2001). Caplan and Chen (2006) have also argued that fMRI is useful for exploring important cognitive operations in the sentence comprehension domain, while Jonides, Nee, and Berman (2006) have made a similar claim studying the cognitive operations and the brain structures involved in an interference-resolution task. Moreover, Cappa (2006) also argued that brain imaging is useful in adjudicating between competing theories when the latter predict, for instance, that either a single process or two different processes are involved in a cognitive task. He also claimed that brain imaging may have a role of "Surrogate Behavioural Marker" in the evaluation of cognitive theories. This would occur when more conventional techniques such as behavioural reaction times fail to show differences in performance. In general terms, according to those who consider neuroimaging useful for learning more about cognition, fMRI is power enough to suggest crucial new behavioral or neuropsychological investigations (Downing et al., 2001) and to lead to the generation of new hypotheses (Seron & Fias, 2006).

As stated before, pessimistic conclusions have however been drawn about the utility of brain imaging. Thus, according to Harley (2004, p. 55) “knowing the hardware underlying something tells us nothing about the software that runs upon that hardware. In either case, we need the model before the pictures”. Harley has also claimed that neuroimaging may at best have a suggestive role, rather than crucial, when it is used in conjunction with cognitive neuropsychology. This is also due to the fact that (see also Vallar, 2006) in many brainimaging studies of normal subjects the brain areas that neuropsychology indicates as being not critically involved in a cognitive task, also tend to activate. In a similar way, Page (2006) has claimed that fMRI tell us nothing about *how* a specific cognitive process is implemented in the brain even though it informs about *where* a cognitive process occurs. In line with Page’s proposal, Coltheart (2004; 2006) suggests that fMRI reveals facts about the brain that, however, do not constraint the natures of information-processing systems, thus making fMRI unhelpful for dissociating alternative cognitive models (see also van Orden & Paap, 1997 for similar arguments).

Shallice’s (2003; 2004) position seems to be particularly important for reconciling fMRI with cognitive neuropsychology (and possibly with cognitive modelling as well). He has claimed that brain imaging, similarly to cognitive neuropsychology, can provide evidence that a specific cognitive domain consists of more than one separable subsystem. He (Shallice, 2003) has also proposed that the critical factor that has to be taken into account when trying to relate analyses of neuropsychology and brain imaging is the cognitive architecture to which such investigations are referred. He also suggests that converging evidence from different methods can be obtained if, for instance, functional descriptions of specific syndromes, obtained through anatomically-based group studies, are also taken into account. According to Shallice (2003), fMRI has been particularly concerned with cognitive systems based on isolable subsytems which have received large consensus also in neuropsychological investigations. On the other hand, he claimed that both fMRI and neuropsychology have been much less concerned with other kinds of functional architecture (connectionism and production systems, but see exceptions reported above).

The present research project aims to provide evidence about how findings from investigations carried out using different methodologies (i.e. neuropsychological single-case analysis and group-study, and fMRI) may be linked together if cognitive models of task performance are made explicit. As proposed by Shallice (2003), this seems to be a valuable enterprise particularly in poorly understood cognitive domains, one of which is that involving the higher-level processes of the language production system.

1.1.1. Different approaches to cognitive modelling

Connectionism is the most common approach for modelling processes in different cognitive domains (McClelland, 1992). Models developed within this framework address the parallel nature of many psychological processes. A crucial assumption of connectionism is that properties of neural tissue such as massively parallel computation through the interaction of many simple processing units are critical for understanding how the mind works and in modelling cognitive processes. The major method of connectionism is the use of artificial neural networks. These are simplified models of the brain composed of large numbers of units which represent the analogous of neurons. These units are generally divided into three classes: input units which receive information that has to be processed, output units, and units in between which are known as hidden units. A typical artificial neural network consists also of weights that measure the strength of connections between the units and mimic the effects of the synapses that link one neuron to another. Neural network models have several properties that make them appropriate for cognitive modelling; just to name a few of these, they 1) show graceful degradation of performance in the face of an artificial damage, 2) learn from examples, and 3) generalise the learning to new examples. Once tested artificial neural networks have demonstrated a surprising ability to learn different cognitive skills such as face recognition, reading, and the detection of grammatical structure (see McClelland, 1992, and Cooper, 2002, for general overviews of connectionist models, and Plaut et al., 1996, for a specific model of the reading processes). Damaged connectionist networks (e.g. some nodes are removed or noise is added to activation values) have also shown behaviours similar to those observed in patients with brain damage (Plaut & Shallice, 1993). Connectionist networks can be of different types (see Cooper, 2002 for a brief review), one type being the *interactive activation network*. The nodes of this kind of network can be associated to high level concepts such as word, and they can compete for selection through mechanisms of mutual inhibition and self excitation (McClelland, 1992). As suggested by Cooper (2002), interactive activation networks are particularly suited for modelling tasks that involve conflicts between various interacting sources of information.

Another important approach to cognitive modelling is the use of symbolic cognitive models. Symbolic models assume that information processing can be described in terms of manipulation of symbolic representations. In this view the neural tissues are not of primary importance for understanding cognitive functioning. Symbolic models are generally developed within the framework of production systems (PSs) which started to evolve shortly after the first works of Newell and colleagues (Newell, Shaw, & Simon, 1958) on problem solving. PSs capture the idea that cognitive processing can be expressed through the cyclic application of rules to the current representation of one's beliefs. A PS is a model of cognitive processing, consisting of a collection of *if-then* rules (i.e. production rules) (Anderson & Lebiere, 1998). Each rule has a *condition* part and an *action* part and the logic is that when the condition holds true, then the action is taken. Generally, a PS includes two main components: the production memory (which holds the production rules that refers both to general knowledge and to task-specific knowledge), and the propositional memory (which holds a propositional database) which may be referred to as the working memory of the PS. The PS operates in a cyclic *recognise-act* fashion. First, in the *recognise phase* a rule whose conditions are satisfied is identified. Then, in the *act phase* that rule is fired (i.e. an action is carried out), and specific propositions may be added or deleted to or from working memory. This in turn reflects in another rule whose conditions are satisfied, so that the cycle repeats. Processing terminates either when no rule is identified in the recognise phase or when a fired rule signals the end of processing. PSs have also some key properties that make them appropriate for modelling cognition. First, they allow both parallel and serial processing since many production rules occurs in parallel in the recognise phase, but only one production at time can fire in the act phase. Second, a PS entails flexible control of the information processing. This means that if relevant information appears in working memory, a PS can abandon its current line of processing following a new line.

An important feature of most PSs is the way in which they handle with *conflicts* which may occur when more than one production rule has its conditions satisfied at a given time. Important mechanisms of conflict resolution, (i.e. one production is chosen from among others) may be to select: 1) productions whose conditions match most recently created contents of working memory, 2) productions with the highest value of activation, or also 3) more complex productions (consisting of many conditions) relative to simpler productions since the former are more likely to be specific for the current task situation (Anderson & Lebiere, 1998; Cooper, 2002).

Since the 1990s, cognitive architectures have been proposed as another approach to cognitive modelling (Newell, 1990). A cognitive architecture represents a unified theory of cognition in which a complete organization of the information processing mechanisms of the mind/brain is made explicit through the creation of specific models. Cognitive architectures may include several subsystems such as long-term memory, working memory, production systems, motor and perceptual systems, and learning mechanisms. Models of cognitive tasks which are developed within a cognitive architecture have to specify how these subsystems interact and provide the architecture with the appropriate task-specific knowledge (e.g. a series of production rules). Nowadays there are several cognitive architectures such as Soar (Newell, 1990), EPIC (Meyer & Kieras, 1997), CAP (Schneider & Oliver, 1991), and ACT-R which is become the most popular (Anderson & Lebiere, 1998; Anderson et al., 2004). ACT-R is an hybrid architecture since it contains both subsymbolic and symbolic aspects. The latter are given by the use of a PS component while the former are given by activation values of working memory elements (i.e. chunks) and by utility values of production rules that may influence the probability of selection of, respectively, chunks and productions.

More recently, an integrated language for cognitive modelling has been proposed (COGENT, Cooper & Fox, 1998; Cooper 2002) which supports many of the different styles of modelling briefly described above. COGENT does not embody any particular theory of the cognitive architecture, but it provides a set of primitives (such as PS, connectionist networks, and memory buffers) which may be rigorously assembled, in a box and arrow notation, to implement a variety of computational models of different cognitive domains. In a COGENT model it is generally assumed that boxes correspond to functional components of cognitive processes, so that a correspondence would exist between the states of these components and the mental states. An important aspect of COGENT, that makes it particularly flexible, is that boxes may be configured through the use of properties such as capacity limitations and decay for memory buffers and rate of firing for production rules. Specific manipulations of properties may allow ideal performance on a task to degrade, potentially mimicking pathological neuropsychological conditions.

1.2. Fronto-striatal circuits: Anatomo-functional considerations

The frontal lobes are the most anterior part of human brain. They are separated from the temporal lobes by the Sylvian fissure, and from the parietal lobes by the central sulcus.

The frontal lobes can be roughly distinguished in two parts: the prefrontal cortex (PFC), which represents the rostral part, and the motor, premotor and supplementary motor areas, which form the more posterior part of the frontal lobes. PFC has a modular structure, as several areas are differentiated on the basis of cyto-architectonic criteria (Brodmann, 1909; Preuss & Goldman-Rakic, 1991; Petrides & Pandya, 1994), and of distinct connections with other cortical and subcortical regions (e.g., Schmahmann & Pandya, 1997). PFC can be anatomically classified in three parts (Fuster, 1999): the lateral PFC (Brodmann areas (BA) 8, 9, 10, 11, 44, 45, 46, and 47), the orbitofrontal cortex (OFC, BA 10, 11, 13, and 47), and the medial PFC (BA 8, 9, 10, 11, 12, 25, and 32).

It has been well-established for more than two decades (Alexander, DeLong, & Strick, 1986) that the frontal lobes are functionally associated to the basal ganglia (BG). The BG are a network of neuronal elements whose main components are the striatum, the pallidum, the substantia nigra, and the subthalamic nucleus (Parent & Hazrati, 1995). The striatum can in turn be divided in neostriatum (i.e. caudate nucleus and putamen) and ventral striatum (including the nucleus accumbens) (Alexander et al., 1986; Postuma & Dagher, 2006). Interest in the BG has been originally motivated by the striking motor symptoms which occur in specific pathological conditions after lesions involving these structures. Lesion at BG levels can in fact lead in humans to disorders that range from hypokinetic (e.g. Parkinson's disease) to hyperkinetic dysfunctions (e.g. Huntington's chorea) (Parent & Hazrati, 1995). In this view BG structures were initially thought to operate mainly in the domain of motor control (Mink, 1996; Middleton & Strick, 2000).

However, it is now accepted that the BG are also involved in nonmotor cognitve functions (Owen, Doyon, Dagher, Sadikot, & Evans, 1998; Saint-Cyr, 2003; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Postuma & Dagher, 2006). Alexander and colleagues (1986) suggested that the BG influence a broad range of behaviour being involved, with frontal lobes, in 5 segregated parallel loops (see figure 1). The functional specialization of these loops relates to motor, oculomotor, cognitive, lexical-grammatical, and emotional domains. According to this view, each striatal area receives input from a different area of the cortex and projects back to these areas via specific BG nuclei and the thalamus. Minor modifications to the proposal of Alexander and colleagues have been advanced more recently by Lawrence, Sahakian, and Robbins (1998), while others (Parent & Hazrati, 1995; Postuma & Dagher, 2006) have identified 3 different functional zones of the striatum (associative, sensorimotor, and limbic striatum), which receives input from different cortical areas. Recent evidence (Saint-Cyr, 2003) suggests also that the loops may not be totally segregated given the presence of overlapping projections which leave the thalamus for the cortex.

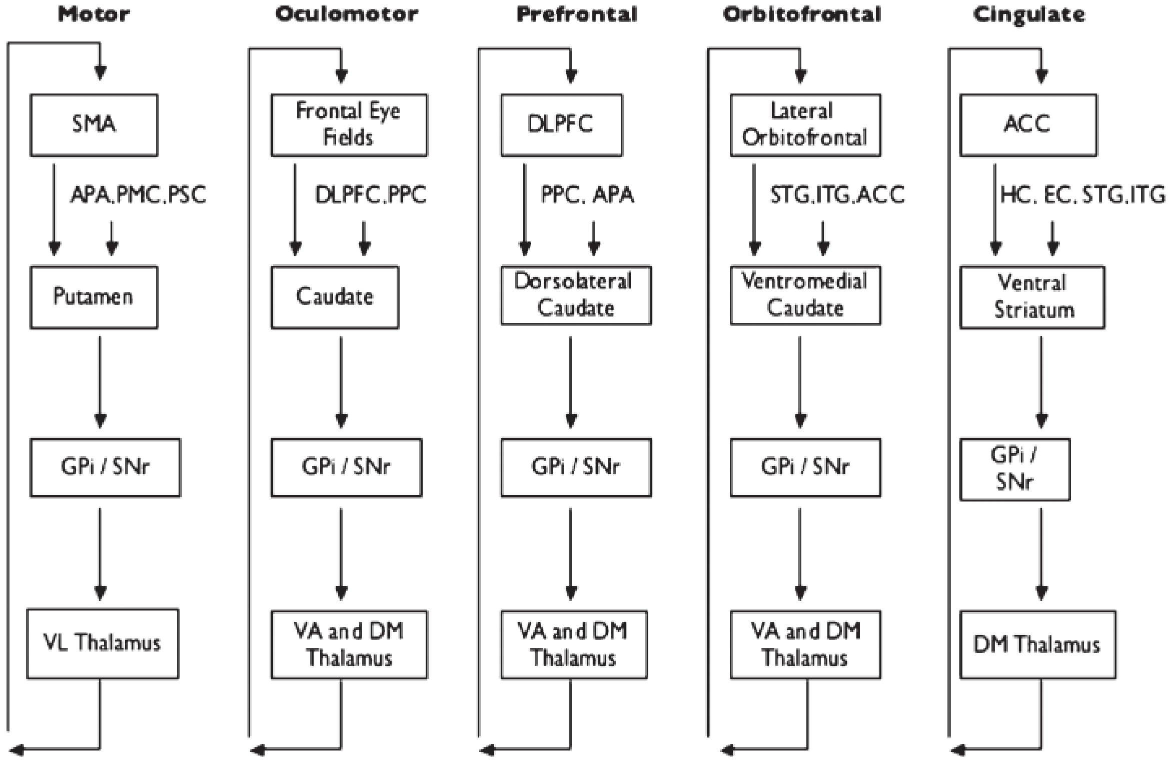

Figure 1.1: Parallel loop models of corticostriatal connectivity (Postuma & Dagher, 2006; original version by Alexander et al., 1986). SMA, supplementary motor area; APA, arcuate premotor area; PMC, primary motor cortex; PSC, primary somatosensory cortex; PPC, posterior parietal cortex; STG, superior temporal gyrus; ITG, inferior temporal gyrus; ACC, anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; HC, hippocampus; EC, entorhinal cortex; GPi, globus pallidus interna; SNr,substantia nigra pars reticulata; VL,ventrolateral; VA,ventroanterior; DM,dorsomedial.

The projections from cortical areas to the BG are mediated by the neurotransmitter glutamate. The connections between the striatum and the inner globus pallidus-substantia nigra (pars reticulata) complex are divided into two pathways: the direct pathway and the indirect pathway. The latter goes through the external globus pallidus and the subthalamic nucleus using mainly GABA as neurotransmitter. The subthalamic nucleus projects in turn to the inner globus pallidus-substantia nigra (pars reticulata) complex using glutamate. In the direct pathways the striatum projects to the globus pallidus-substantia nigra (pars reticulata) complex using substance P and GABA as neurotransmitters. Efferent GABA-ergic projections leave the globus pallidus (internal)-substantia nigra (pars reticulata) complex for the thalamus. Finally, thalamic nuclei project back into specific regions of the frontal cortex using glutamate. There is a delicate balance between the direct and indirect pathways that is partly maintained by dopamine release from the substantia nigra pars compacta (SNp) directly to the striatum. Dopamine release inhibits the indirect pathway by stimulating dopamine D2 striatal receptors, and excites the direct pathway by stimulating the dopamine D1 receptor. The direct route is thought to be responsible for the initiation of actions while the indirect pathway for braking or switching from one action to the next. As it will be explained in more detail in chapter 4, dopamine deficiency may be the cause of many pathological conditions, one of the most common being Parkinson's disease (PD). This condition is associated to a depletion of dopamine in the substantia nigra pars compacta which disbalances the direct and indirect pathways from the striatum, giving rise to an enhanced excitation of the subthalamic nucleus and the globus pallidus internus, and, as a consequence, also to an increased inhibition of the thalamus. As final result the frontal cortex may be less activated in PD. Thus, globally BG circuits are considered to control the excitability of the frontal lobes (Lawrence et al., 1998; Saint-Cyr, 2003; Postuma & Dagher, 2006).

1.2.1. Executive functions and fronto-striatal circuits

Executive functions are mechanisms aimed to guide thought and behaviour in accordance with internally generated goals or plans (Shallice, 1988; Miller & Cohen, 2001; Royall et al., 2002; Stuss & Knight, 2002). Executive functions are often invoked when it is necessary to override responses that may otherwise be automatically elicited by stimuli in the external environment. Although some researchers have proposed that various PFC areas have an equipotential and undifferentiated role (e.g., Kimberg & Farah, 1993; Duncan, Burgess, & Emslie, 1995; Duncan, 2005), there is now a large consensus suggesting that the executive system can be differentiated into several relatively independent functions (e.g. Smith & Jonides, 1999; Stuss et al., 2005; Alexander, Stuss, Picton, Shallice, & Gillingham, 2007; Persson, Welsh, Jonides, & Reuter-Lorenz, 2007; Shallice, Stuss, Alexander, Picton, & Derkzen, 2008; Shallice, Stuss, Picton, Alexander, & Gillingham, 2008). Moreover, recent neuroimaging and neuropsychological findings also suggest that these functions may be localized in discrete parts of the PFC (Persson et al., 2007; Alexander et al., 2007; Shallice, Stuss, Picton et al., 2008).

The frontal lobes have been associated with the higher executive functions since at least the famous case of Phineas Cage (Harlow, 1848), whose personality changed dramatically after that his frontal lobes were damaged as consequence of an accident occurred at work.

Furthermore, technologies such as single-cell recordings, neuroimaging, and fine-grained lesion analyses suggest that several aspects of the PFC contribute to its role in mediating executive functions (Royall et al., 2002). First, PFC is connected to more brain regions than any other cortical region. Second, PFC receives direct cortical input only from heteromodal association areas and this allows the PFC to act on information that has already been processed at lower levels. Third, changes in firing of frontal cortex neurons can be determined by a manipulation of the motivational importance of environmental stimuli. Fourth, PFC is also strongly interconnected with the limbic system. Moreover, as reported in the previous section, PFC is also the main target for projection coming from the thalamus. Thus, PFC is the only region which can integrate cognitive, emotional, and sensorimotor information with internal motivation in order to reflect goal-directed behaviour (Royall et al., 2002; Hasselmo, 2005). In this view PFC has been considered to be involved in "top-down" processing, that is when "the mappings between sensory inputs, thoughts, and action are weakly established relative to other existing ones or rapidly changing" (Miller & Cohen, 2001, p.168). As it will be reported in more detail in the next section, there is converging evidence showing that PFC can actually maintain goal-relevant information even in the face of distractors (Fuster, 1995; Goldman-Rakic, 1996; Miller, Erickson, & Desimone, 1996; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997).

One of the most influential models which aims to explain the functions of the PFC is the Supervisory Attentional System (SAS) model (Norman & Shallice, 1980; 1986; Shallice, 1988). This is grounded in the dichotomy between automatic versus controlled processes which was first proposed in the domain of attention research (Shiffrin & Schneider, 1977a; 1977b) and then extended to the whole human information processing system (e.g. Jonides, Naveh-Benjamin, & Palmer, 1985). Important features of automatic processes are that they are elicited by appropriate inputs, do not require effort, are fast, and do not suffer from dual-task interference; by contrast, controlled processes are effortful, suffer from dual-task interference, and are slower as they begin with an act of the will (see also Badre & Wagner, 2002 for a similar position in the domain of retrieval of semantic information).

Norman and Shallice's proposal (1980; 1986) postulates the existence of two systems: *contention scheduling*, which produces automatic processes, and the SAS that is a high-level system which deals with controlled processes. In the contention scheduling over-learned responses (i.e. schemata), compete against each other for the control of perceptual and motor systems. Schemata can be active to a different degree depending on the associative strength of each schema with internal or external triggers and with specific patterns of behaviour.

Complex activities, such as driving a car, can be executed appropriately by the contention scheduling although in a rather automatic fashion. Important features of schemata are that they are rigid, need extensive time and practice to develop, and do not generalize easily to novel situations. The main task of the SAS is to bias the selections of schemata in the contention scheduling in novel or non-routine situations. Thus the SAS is important both in the implementation and monitoring of new schemata and in inhibiting prepotent schemata which are irrelevant in the current situation (Shallice & Burgess, 1996).

Stuss and colleagues have provided a considerable amount of evidence in favour of a fractionation of attentional processes within PFC (Stuss, Shallice, Alexander, & Picton, 1995; Stuss et al., 2005; Alexander, Stuss, Shallice, Picton, & Gillingham, 2005; Shallice, Stuss, Picton et al., 2008). In particular they defined which attentional processes may characterize the SAS. Some of the identified processes are: *energizing schemata*, which can be considered as the allocation of arousal’s energy to the neural systems required to perform a given task; *task-setting*, that is the process of representing the task demands in an early stage of performance in order to accomplish them appropriately; *inhibiting task-irrelevant schemata*, as required when an infrequent but prepotent response should not be executed; *monitoring behaviour* in order to adjust the level of activity in schemata accordingly. In line with the proposal of Stuss and colleagues, these processes do not coincide with precise tasks, but underlie performance of several apparently different tasks.

As already shown, the frontal lobes are extensively connected to the BG and this indicates that also these structures may have an active role in many SAS processes. In fact there is evidence that subcortical lesions can affect executive functions either directly or indirectly via frontal cortical metabolic changes (e.g. hypoperfusion, Nadeau & Crosson 1997; Hillis et al., 2002). In the latter view the impairments in executive functioning which are sometimes found in non-demented patients suffering from subcortical lesions are due to disturbance of subcortical-frontal circuits (Kramer, Reed, Mungas, Weiner, & Chui, 2002). Three fronto-striatal circuits are thought to be particularly relevant to executive control (see figure 1): the dorsolateral prefrontal circuit, the lateral orbitofrontal circuit, and the anterior cingulate circuit (Alexander et al., 1986; Mega & Cummings, 1994; Lawrence et al., 1998). The first of these is involved in many higher cognitive functions such as goal setting (Rogers et al., 1998; Meiran, Friedman, & Yehene, 2004), planning and sequencing (Saint-Cyr, 2003), response set formation (Fletcher, Shallice, & Dolan, 2000; Nathaniel-James & Frith, 2002), set shifting (Shallice, Stuss, Picton et al., 2008), verbal and spatial working memory, and monitoring (Stuss et al., 2005). Moreover, components of this circuit such as the DLPFC have been held to be critically implicated in response suppression during the random number generation task (Brown, Soliveri, & Jahanshahi, 1998, Jahanshahi et al., 1998) and also during other tasks requiring challenging response inhibition such as the Stroop task (Alexander et al., 2007). The lateral orbitofrontal circuit involves also the ventral anterior and inferior lateral regions of the frontal lobe (BA 10-15, 45 and 47) and it has been argued to be implicated in initiation of internally driven behaviours, in response selection (Thompson-Schill et al., 1997; Thompson-Schill et al., 1998), in setting stimulus-response (S-R) criteria (Alexander et al., 2007), as well as in risk assessment (Rogers et al., 1999).The anterior cingulate circuit is instead claimed to be important in monitoring behaviour, conflict detection and error correction (Peterson et al., 1999; Barch, Braver, Sabb, & Noll, 2000), and in sustaining S-R contingencies (e.g. energization; Stuss et al., 2005; Picton et al., 2007).

Computational models have also investigated the role of fronto-striatal circuits in executive functions. Thus Frank, Loughry, and O’Reilly (2001) have proposed a connectionist model which was aimed to explain how frontal cortex and BG contribute to both updating and maintenance of representations in working memory. The authors have claimed that BG operate a *dynamic gating function* which reflects in the updating of representations in frontal cortex that, in turn, is more critically involved in the active maintenance of such representations. More recently O’Reilly and Frank (2006) have improved their initial proposal including a learning mechanism to their model. Such an addition allowed the model to learn which representations needed to be updated and which maintained. Reinforcement learning mechanisms (thought to be subserved by BG, e.g. Joel, Niv, & Ruppin, 2002) were critical in consolidating the dynamic gating function of the BG which allowed only task-relevant information to be efficiently maintained in PFC.

Another model which investigated the way in which BG and PFC subserve executive functions is that of Amos (2000). He exploited a well-known task which taps executive function abilities, the Wisconsin Card Sort Test (WCST) task, to test his artificial neural network. The WCST requires subjects to sort a deck of cards according to different criteria which are not told in advance to the subjects, namely color, shape, and number which change every so after. Amos’s model was aimed to simulate the impaired performance observed in different clinical populations (Parkinson’s disease patients, Huntington’s disease patients and frontal damage patients) on the WCST test. He found that a lesion to the units of the model which represented frontal neurons led to the production of perseverative errors, in line with what is found in patients with frontal damage or schizophrenic patients (e.g. Waddington et al., 1995); by contrast, a lesion to the units which represented striatal neurons gave rise to random errors, as it is often found in patients suffering from striatal lesions (e.g. Caltagirone, Carlesimo, Nocentini, & Vicari, 1994). According to Amos (2000) the striatum performs a pattern matching operation. This proposal is based on evidence showing that projections to the striatum are topographically arranged such that distributed areas of the cortex, dedicated to the represention of different aspects of the same construct, project to the same area of the striatum. Projections from the striatum are also topographically organized (Graybiel & Kimura, 1995) suggesting that this structure operates to integrate and gate information. Amos claimed that random errors on the WCST are associated to defective mechanisms of matching in the striatum.

The importance of the interaction between BG and PFC is also stressed in the cognitive architecture of Anderson and colleagues (Anderson & Lebiere, 1998; Anderson et al., 2004). In a similar way to Amos's proposal, in ACT-R too, the striatum serves a pattern matching operation. In more detail, this structure is devoted to search for a production rule that matches the current state of the buffers, for instance of the goal buffer which ACT-R assumes to be located in the DLPFC (Anderson et al., 2004). Moreover, in Anderson et al.'s view, the pallidum serves a conflict-resolution function since only a single production can be executed at a given moment in ACT-R, and the thalamus controls the execution of production actions which have the effects of changing the contents of buffers.

Important roles of BG in higher-level cognitive functions have also been suggested based on findings both of neuroimaging and neuropsychological investigations (Rogers et al., 1998; Copland, Chenery, & Murdoch, 2000a; 2000b; Grossman, Lee, Morris, Stern, & Hurtig, 2002; Rissman, Eliassen, & Blumstein, 2003; Crosson et al., 2003; Copland, 2003; Longworth et al., 2005). Thus, there is evidence showing that the dopaminergic dysfunction associated with PD may differentially affect some SAS processes. For instance some studies have been reported as showing that PD patients have depleted attentional resources (e.g. Woodward, Bub, & Hunter, 2002), while others have claimed that these patients are more impaired in the strategic allocation of the resources rather than suffering from a non-specific reduction or depletion (Robertson, Hazlewood, & Rawson, 1996). Moreover Partiot et al. (1996) have shown that PD patients had deficits in re-engaging attention after a shift and in maintaining new task-rules in a delayed response paradigm in which cues could either explicitly indicate the correct answers (externally guided task) or not (internally driven task). In a similar way, Gauntlett-Gilbert, Roberts, and Brown (1999) have shown that PD patients suffered from an inflexible exaggeration of selective attention that remained focused on the previously relevant dimensions of the task in shift situations.

As will be explained in more detail in the next section, different studies have proposed that deficits in the SAS may also be reflected in poor performance on tasks requiring inhibition of prepotent or irrelevant responses; some of these studies have shown that damages to the BG are particularly important in causing failure of inhibition (see Brown et al., 1998; and Castner et al., 2007 for findings obtained on tasks respectively of random number generation and lexical decision). As far as the process of energizing-schemata is concerned, no study has directly investigated whether and to what extent this process is impaired in the pathological conditions which affect the BG. However, it has been argued that the striatopallidal complex is involved in a condition known as Auto-Activation deficit (AAD; Laplane & Dubois, 2001) which is similar to the most dramatic manifestation of deficient energizing, namely akinetic mutism (see Stuss et al., 2005; see also Alexander, 2001 for evidence showing that akinetic mutism responds to dopaminergic treatment including Levodopa). The main symptom of AAD is represented by inertia (or "mental emptiness" as often reported by the patients) whereby patients tend to stay in the same place all day long, without taking any initiative or engaging in spontaneous activity. According to Laplane and Dubois (2001), the patients affected by AAD have deficits in the spontaneous activation of mental processing which extend to many different cognitive domains. These authors have proposed that the BG operate to activate, initiate, and maintain responses ("to energise the appropriate group of muscles", Laplace & Dubois, 2001; p. 812). Finally, patients with damage to BG have been found to be impaired in tasks which investigated working memory and memory retrieval abilities (Owen, Iddon, Hodges, & Robbins, 1997; see also Lewis, Slabosz, Robbins, Barker, & Owen, 2005; Filoteo et al., 1997).

As already mentioned this thesis is about selection of task-relevant responses. Thus, in the next section we report evidence about the way in which fronto-striatal circuits control the retrieval and selection of responses in a task-relevant manner.

1.3. Selection of task-relevant information and fronto-striatal circuits

As already mentioned, the human ability to select relevant from irrelevant information is necessary in order to adapt to the complex environment we live in. According to Thompson-Schill, Kan, and Oliver, (2006, p. 20) "in any model in which information is represented as a distributed pattern across multiple units, there exists the possibility for the partial activation of multiple, incompatible representations. The process of resolving this conflict and arriving at a stable representation can be referred to by the term *selection*". As briefly described above, PFC has been thought to enable flexible and context-sensitive responses and to favor task-relevant representations even in the presence of prepotent, task-irrelevant information (Shallice, 1988; Miller & Cohen, 2001; Gazzaniga et al., 2002; Badre & Wagner, 2002). Similarly it has been proposed that prefrontal cortex mediates the selection of action by the weighting of information active in working memory (Kimberg & Farah 1993); a position similar to the "dynamic filtering" mechanism proposed by Shimamura (2000) whereby prefrontal cortex selects information most relevant for meeting the demands of a task. Accordingly, one or more attentional components of the SAS allow subjects to modify the salience of information depending on their goals (Norman & Shallice, 1980; 1986).

The relationship between PFC and selection of task-relevant responses has been addressed in a series of studies by Thompson-Schill and colleagues (Thompson-Schill et al., 1997; 1998). In 1997 these authors tested the dynamic filtering hypothesis using three semantic tasks. The critical variable was the selection demands that were varied across the conditions of each task. In a first task, Thompson-Schill and colleagues (1997) investigated the production of verbs from noun-cues in conditions of either low or high selection (i.e., either when one verb, *apple → eat,* or at least two verbs, *map → travel, find,* were elicited by the stimulus, respectively). In a classification task, subjects classified line drawings of common objects according to either one of eight different attributes (high selection) or to a basic level object name (e.g. spider, hammer). A comparison task was also used in which subjects had to compare a target word to several probe words and decided which probe was most similar. In the high selection condition comparisons were based on specific attributes (e.g. color, shape, function) while, in the low selection condition, comparisons were based on global similarity. With regard to the first task, that is the verb generation task, the authors claimed that, in response to cues such as *map,* the activation of many weakly associated actions may fail to produce sufficient activation to select any action representation. Thompson-Schill et al. argued that these situations can cause conflict among active representations in working memory which require top-down intervention. On the other hand, in response to cues such as *apple,* the strongly-associated action *eat* might be activated from the input without additional demands for conflict resolution. Thus, they claimed that the process of generating a verb related to *map* and *apple* differs in their selection demands. Importantly, the authors found slower RTs and an increased activation of the left inferior frontal gyrus (LIFG) in the high selection condition of each task. They interpreted these results as suggesting that the LIFG is involved in response selection. In a subsequent study, Thompson-Schill et al. (1998) showed that lesions to the LIFG were associated with difficulties in producing verbs primarily in the high selection condition, confirming the critical role of the LIFG in selection from among alternative responses. More recent studies have confirmed these findings about the LIFG, both using the same paradigm of verb generation of Thompson-Schill and colleagues (i.e. Persson et al. 2004), and other related paradigms (Barch et al., 2000; Moss et al., 2005). Neuropsychological findings, too, have suggested that the LIFG plays a crucial role in the selection of a response from among competing sources of information (see chapter 2, see also Robinson, Blair, & Cipolotti, 1998; Robinson, Shallice, & Cipolotti, 2005).

There is also evidence that the potential role of the LIFG in the selection between alternative responses may not be limited to semantic retrieval tasks, reflecting instead a more general mechanism of the PFC required for the selection of responses from memory (Zhang, Feng, Fox, Gao, & Tan 2004). Despite this evidence, the role of the LIFG in selection of responses from among alternative options has been recently questioned particularly in the domain of verb production. As will be discussed in more detail in chapter 4, there is an alternative view about the role of the LIFG in this task, namely one that this area is important in semantically controlled retrieval. Such a process would be needed particularly when no verb response is strongly associated to a given cue-stimulus (Martin & Byrne, 2006; Martin & Cheng, 2006). Thus, according to this view a weak stimulus-response association would maximally involve the operations of the LIFG irrespective of whether or not competition between alternative verb-responses is elicited by a cue-stimulus.

Recently, Badre and colleagues (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner, 2005; see also Badre & Wagner, 2002) attempted to reconcile the selection and association strength accounts for LIFG function, providing fMRI evidence of some functional segregation within this regions; in particular they showed that the left mid-ventro lateral prefrontal cortex (VLPFC, inferior frontal gyrus pars triangularis and pars opercularis, BA 44/45) was actually involved in selecting a response from among others in competition. By contrast, the more anterior section of the VLPFC (including the inferior frontal gyrus pars orbitalis, BA 47) activated more during controlled retrieval.

The studies briefly described above indicate that semantic retrieval may give rise to conflicts between multiple responses. The issue of *how* selection of task-relevant information occurs thus becomes an important one. Selection can occur in at least two different ways. A first possibility would be to accentuate the relevant information while the second would be to selectively exclude (i.e. inhibit) irrelevant information. The two mechanisms are not mutually exclusive as suggested by the process of selection of a response in an interactive activation system (e.g. McClelland & Rumelhart, 1981; see also chapter 3); for instance if we have fixed cognitive resources, the allocation of these to one piece of information represents a limit for those allocated to other information (Gazzaniga et al., 2002). Indeed, Mostofsky and Simmonds (2008) have recently proposed that response inhibition and response selection are similar mechanisms both depending on fronto-striatal circuits and in particular on the circuit involving the pre-supplementary motor area (pre-SMA; see also Picton et al., 2007). According to the authors, components of these circuits select to engage relevant responses and to inhibit irrelevant ones. In other words, response inhibition involves the suppression of a prepotent, irrelevant response that would correspond to select not to respond.

A more direct role of inhibitory mechanisms in the selection of responses has been proposed by Levy and Anderson (2002). These authors have claimed that the ability to control memory represents an instantiation of response-override situations that are likely to require executive control. Response-override situations are those in which one has to stop an habitual response to a stimulus because of another, less habitual, is more relevant in the current situation. One candidate solution for response-override is to suppress the more habitual response in order to select the less habitual one. Accordingly, Levy and Anderson (2002) have proposed that inhibitory mechanisms, which they claim to be generally subserved by PFC and anterior cingulate cortex, act in two memory situations, namely when prepotent responses must be inhibited and when one needs to select between alternatives during retrieval. Generally speaking, inhibitory control is an important function of frontal lobes (Norman & Shallice, 1986; Gazzaniga et al., 2002), and the inability of patients with frontal lobe damage to inhibit irrelevant information, for instance in the Stroop test and in the go-nogo task (Alexander et al., 2007; Picton et al., 2007, respectively), is a key demonstration of such an ability.

As stated above, selection of task-relevant responses may also occur through an accentuation of relevant responses. Such a possibility has been suggested by Egner and Hirsch (2005) who have claimed that resolution of conflicts between incompatible responses is mediated by a top-down amplification of cortical responses to task-relevant information rather than inhibiting task-irrelevant information. The authors used fMRI while subjects were engaged in a modified version of the Stroop task in which the level of conflict was varied using face stimuli of actors or politicians. Each face was presented together with either a category-congruent or category-incongruent name of other actors or politicians. The level of congruency of the previous trial gave the level of control required by the current trial while the current-trial congruency determined the level of conflict on the current trial. Egner and Hirsch's factorial design involved the following four conditions which implied different levels of control and conflict: successive congruent-congruent trials reflected low conflict and low control; congruent-incongruent trials reflected high conflict and low control; incongruent-congruent trials reflected low conflict and high control; and incongruent-incongruent trials reflected high conflict and high control. Subjects had to discriminate actors from politicians in a two-alternative forced-choice design. In one condition they had to judge the face stimuli while in the second they had to ignore the faces and judge the written names. Egner and Hirsch (2005) found that face processing was amplified when control was high relative to when it was low. More specifically, they obtained that activation in the fusiform face area (FFA) in response to face-target stimuli, was increased on incongruent trials which followed other incongruent trials (High conflict-High control) relative to the high conflict-low control condition. Moreover, they tested the hypothesis that the amplification of face processing in the FFA was driven by input from dorsolateral prefrontal cortex (DLPFC) which is known to be important in cognitive control. A psychophysiological interaction analysis (PPI) showed that functional coupling between the DLPFC and the FFA increased under high control in the face-target condition, but not in the face distracter condition.

Other studies have focused more on the role that the BG, and more generally fronto-striatal circuits, have in the selection of task-relevant information giving a more general explanation of this executive process. Thus McNab and Klingberg (2008) have stressed the functional coupling between PFC and BG and proposed that they operate in concert to filter irrelevant information. In particular they claimed that globus pallidus is important for allowing only relevant information to enter working memory. A position similar to that of McNab and Klingberg is that of Frank and colleagues (2001) and O’Reilly and Frank (2006) that we briefly described in the previous section. According to these authors, the BG enables working memory representations in frontal cortex to be updated in a task-relevant fashion. Furthermore, more than two decades ago Norman & Shallice, (1986; see also Robbins & Sahakian, 1983) had proposed a mechanism, which shares similarities with some of the proposals reported above (e.g. Egner & Hirsch, 2005), through which task-relevant responses may be accessed. These authors claimed that the BG may operate to potentiate the activation level of schemas in contention scheduling thus biasing their selection in a task-relevant manner. The validity of such a proposal has been confirmed more recently by results of an fMRI study of language production carried out by Crosson et al., (2003). These authors have in fact proposed that the BG maintain a bias toward a lexical alternative chosen from among others in competition during controlled word selection.

From another perspective there is also evidence that the BG have an important role in suppression of competing response alternatives. Such a role in the motor realm is a well-known function of the BG (Mink, 1996). Nevertheless, there have been reported studies (e.g. Copland, 2003; Bouquet, Bonnaud, & Gil, 2003; Longworth et al., 2005; Castner et al., 2007; Crosson, Benjamin, & Levy, 2007) suggesting that Mink's framework can also be applied to domains other than motor behavior (i.e. semantic priming, word selection, cognitive inhibition, working memory). For instance Redgrave, Prescott, and Gurney (1999) have claimed that the BG operate as a selection device to resolve conflicts in different cognitive domains. Accordingly, in the domain of language production, a considerable amount of evidence obtained from both fMRI and neuropsychological studies on patients with subcortical lesions (e.g. Copland et al., 2000a; 2000b; Rossell, Bullmore, Williams, & David, 2001; Copland, 2003; Castner, et al., 2007; Castner et al., 2008), suggests that the BG operate a function of suppression and selection of responses in situations of competition. As an example, Castner et al., (2008) administered noun and verb generation tasks from both noun and verb cue-stimuli to 8 PD patients that had received surgery for deep brain stimulation (DBS) of the subthalamic nucleus (STN). The tasks were to be carried out both when patients were stimulated or without stimulation. In line with an earlier study (Péran et al., 2003), PD patients had a deficit of verb generation when they performed the tasks without being stimulated. However, when patients were stimulated they made more errors in the noun-to-noun and verb-to-verb tasks. Errors in the verb generation task occurred particularly in response to stimuli with high selection demands (i.e. stimuli that were associated with more than a verb response). According to the authors, STN stimulation affected the ability to select between competing alternatives during verb generation.

In a similar fashion, Bouquet et al. (2003) had shown that PD patients were particularly impaired when asked to perform the section B of the Hayling test (Burgess & Shallice, 1996) which requires inhibition of prepotent responses (i.e. inhibition of words to complete phrases). Just to give a few examples in domains other than language production, Dujardin, Degreef, Rogelet, Defebvre, & Destee (1999) have shown that PD patients had problems in inhibiting task-irrelevant information in a modified version of the Stroop test and of the Brown-Peterson paradigm. Moreover, in the domain of task shifting, Pollux and Robertson (2002) have shown that PD patients had longer switching cost (the difference between a switch trial and a repeat trial in a task-switching experiment) relative to normal controls particularly in situations of high interference, namely when selection of relevant responses relied on inhibition of irrelevant responses.

1. 4. The present project

The main aim of this thesis is to investigate the function of the PFC and BG in the selection of task-relevant representations. To that end, we have used different tasks and methodologies in the domain of the higher levels of the language production system.

The ability to select relevant responses in situations of high interference can be dramatically disrupted after brain damage. Within the language domain this is what has been suggested to happen in dynamic aphasia (Robinson et al., 1998; Robinson et al., 2005; 2006). This is a disorder in which patients have an exceptionally reduced spontaneous speech in the context of well-preserved naming, articulation, prosody and repetition skills (Luria, 1973). As part of this project there was the opportunity to study a patient with dynamic aphasia following a subcortical lesion. We carried out a single case analysis of this patient (chapter 2) aiming to investigate his ability to select responses from among alternatives. This was done both within and beyond the domain of language to test the hypothesis that subcortical lesions which give rise to dynamic aphasia also lead to deficit in non-verbal domains. The results of the single case analysis motivated us to investigate the ability of selecting responses from among alternatives in normal adult subjects (second part of chapter 2) and also to explicitly produce a model of the processes of conceptual preparation of language production (chapter 3). The aim of the model is twofold: to give one of the first implementation of the higher-levels of the language production system and to simulate dynamic aphasia.

The difficulty our patient had in generating novel thoughts and his inability to select a verbal response between other alternative options, further stimulated our interest to study how fronto-striatal circuits may handle the processes of retrieving and selecting task-relevant responses in the language domain. Three studies were carried out on this topic and are reported in the second part of the thesis. In an initial study (chapter 4) we have investigated associative retrieval of nouns and verbs in populations of healthy older subjects and PD patients. Currently, there is a debate on whether competition between alternative responses or association strength is the critical factor explaining performance in the verb generation task. In this study we used a paradigm (Martin & Cheng, 2006) that allowed the dissociation of the two processes, and we found that both are important in helping to give rise to the poor verb generation performance of PD patients. The second process (i.e. association strength) had however a greater impact on performance than the first (i.e. selection). In a second related study we proposed a cognitive model (chapter 5) which was based on the ACT-R cognitive architecture (Anderson et al., 2004) and on general theories of executive control (Stuss et al., 2005). The model was aimed to give a unitary account of performance in word generation tasks and was tested in a series of simulations in which the performance of young adults, older adults, and PD patients on the noun and verb generation tasks were reproduced.

In a subsequent study we investigated the brain correlates of selection of task-relevant responses using fMRI (chapter 6). We administered normal adult subjects the same paradigm of noun and verb production aiming to directly investigate whether the competitive or the associative account of verb generation is to be preferred with respect to the function of the LIFG. Another important aim of the study was to investigate whether task-irrelevant responses interfere during the production of verb responses.

Finally, in chapter 7 the conclusions of the present investigation are drawn, highlighting the methodological, empirical and theoretical considerations which can be derived from this project.

Chapter 2

2.1. Aim of the single-case study

As already shown in the Introduction, the ability to select responses in situations of high competition can be dramatically disrupted after brain damage. Within the language domain this is what has been suggested to happen in dynamic aphasia. This syndrome consists of an impairment in propositional language production characterized by an exceptionally reduced spontaneous speech in the context of well-preserved naming, articulation, prosody and repetition skills. Patients with dynamic aphasia have great difficulty in the initiation and elaboration of self-generated utterances; nevertheless they may be able to describe pictures and to answer certain types of direct questions (Luria, 1973; Robinson et al., 1998; Robinson et al., 2005). Dynamic aphasia generally occurs after lesions confined to the left cerebral hemisphere specifically involving frontal regions; nonetheless rare cases of dynamic aphasia have been described after ischemic lesions involving subcortical structures such as basal ganglia (BG) (e.g. Gold et al., 1997).

In the present investigation we describe a new case of dynamic aphasia, OTM, who was classified as dynamic aphasic following a vascular accident occurred to his left BG (see figure 2.1). In our investigation we have presented a patient with subcortical damage with a series of tasks, commonly used with other dynamic aphasic patients, which tap the ability to select verbal responses from among competing options. We have also extended the investigation to domain other than language in order to test OTM's abilities to generate non-verbal responses. Globally, the case of OTM is particularly relevant to the status of dynamic aphasia as a language specific disorder and on whether functionally distinct sub-varieties of this syndrome exist, as has been suggested by Robinson and colleagues (2005, 2006). Moreover, a careful examination of his extra-language cognitive processes allowed us also to test the hypothesis that subcortical lesions which give rise to dynamic aphasia also lead to deficits in non-verbal domains, as suggested by others (Gold et al., 1997; Raymer, Rowland, Haley, & Crosson, 2002; Robinson et al., 2006). Such a hypothesis would rest on evidence which shows that the role of BG in response selection and inhibition is not restricted to language but also extends to other cognitive domains (e.g. Longworth et al., 2005). Accordingly, as already shown, the involvement of BG in multiple fronto-striatal loops suggests that they may influence a wide range of behaviors (Alexander et al., 1986; Lawrence et al., 1998; Postuma & Dagher, 2006).

The analysis of our single case has brought interesting and clear-cut results that indicate that different sub-varieties of dynamic aphasia exist and that subcortical lesions which give rise to dynamic aphasia also lead to deficits in non-verbal domains. OTM showed indeed a deficit in novel thought generation which involved functions both within and beyond the domain of language..Globally, the findings on OTM have shown that fronto-striatal circuits are crucially involved in response selection and inhibition.

2.1.1. Theoretical accounts of dynamic aphasia

Several theoretical accounts for dynamic aphasia have been proposed. Most of these accounts interpret the syndrome within the domain of language while other explanations extend beyond this domain. Among the accounts that interpret dynamic aphasia within the domain of language there are the general explanations put forward by Luria (1973) and Costello and Warrington (1989). Briefly, according to Luria dynamic aphasia is the consequence of damage to a mechanism aimed to form the linear scheme of a sentence, while Costello and Warrington (1989) have proposed that the syndrome is due to defective mechanisms of verbal planning. Recent investigations of patients with dynamic aphasia (e.g. Robinson et al., 1998; Warren, Warren, Fox, & Warrington 2003; Robinson et al., 2005, 2006) have however shown that both Luria and Costello and Warrington’s accounts are problematic given that they predict the patients to have more generalized verbal generation impairments than those that they actually show. Recently, more specific accounts for dynamic aphasia have been proposed that consider the disorder as due to a specific impairment in creating preverbal messages, following the theoretical framework proposed by Levelt (1989; 1999). Preverbal messages consist of conceptual structures expressed in terms of lexical concepts, which are in turn associated with the corresponding words in the language. For example, Warren et al. (2003) described a patient (ADY) with a frontal lobe dementia who was impaired when asked to combine various lexical concepts in order to create a new sentence or a phrase, and particularly when required to retrieve lexical concepts from among others or when asked to link them in new ways.

A similar interpretation has also been advocated by Robinson and colleagues (2005) to account for the language disturbances shown by patient CH who presented with focal atrophy to the left frontal lobe. CH showed a defective conceptual preparation of language, which was particularly evident when lexical concepts had to be generated in condition of high competition, that is, by choosing them from among others equally plausible such as when a subject has to complete a sentence that can be completed in many different ways. According to Robinson et al. (2005) when stimuli activate many verbal response options, selection between them cannot be accomplished by a damaged system; nevertheless, an appropriate response can be produced when lexical concepts are strongly suggested by the context, namely in conditions of low competition. CH’s impairment was shown to be specific to the language domain since an accurate examination of his non-verbal generation abilities showed that these were intact. Robinson et al. (1998) also reported the case of the patient ANG who was seen to be impaired in the selection of a verbal response when there were many competing options.

As stated above, a number of accounts that interpret dynamic aphasia as arising from impairments not limited to the domain of language exist. For instance, Raymer et al. (2002) suggested that the deficits observed in case of dynamic aphasia may also involve the ability to produce non-verbal responses. A more detailed account has been put forward by Gold et al. (1997) who studied a dynamic aphasic patient (CO) who had a bilateral striatocapsular infarction. These authors stressed the importance of the fronto-striatal circuit involving the dorsolateral prefrontal cortex and the dorsolateral caudate in order to take into account the impairments found in their patient. In more detail, CO had decreased spontaneous speech, difficulties in executive functions and, most importantly, was unable to adopt effective strategies for retrieving information from semantic memory. According to Gold et al., (1997) CO’s deficits in concept formation and semantic strategy formation reflected a more general impairment in the ability to organize knowledge in a hierarchical fashion.

Furthermore, Robinson et al. (2006) reported the case of a patient with progressive supranuclear palsy (PSP) who, despite his propositional language impairment, performed well on word and sentence level generation tasks that required a single response, but did not do so on discourse level generation tests and on tasks which tapped his non-verbal generation abilities. More importantly, Robinson and colleagues (2006) drew a distinction between two subtypes of dynamic aphasia. They argued that patients that present with word and sentence level generation deficits have a language specific impairment and generally left inferior frontal gyrus lesions. By contrast, the second type of dynamic aphasia could be associated with bilateral frontal and subcortical damage; the patients affected by this second subtype should present with verbal and non-verbal generation deficits as well as with problems with discourse level generation tests. The authors also claimed that such patients are supposed to be unimpaired in the word and sentence level generation tests.

2.2. OTM: Case study

OTM is a 67-year-old man, right handed, with 8 years of education, who had retired from work as a solderer. In May 2005 he suffered from an ischemic stroke. A CT-scan revealed a lesion involving the left basal ganglia, the corona radiata, and the surrounding white matter. Within the basal ganglia the lesion involved the putamen and extended to the capsule close to the dorsal caudate (see figure 2.1.). A few days after his admittance to the department of Neurology of the *Ospedali Riuniti* in Trieste he had a second stroke, this time concerning the right parietal lobe. When he was discharged he was referred for a neuropsychological evaluation. The testing was carried out at the Neuropsychology Lab of the Ospedali Riuniti in Trieste over a series of sessions that took place between September and October 2005.

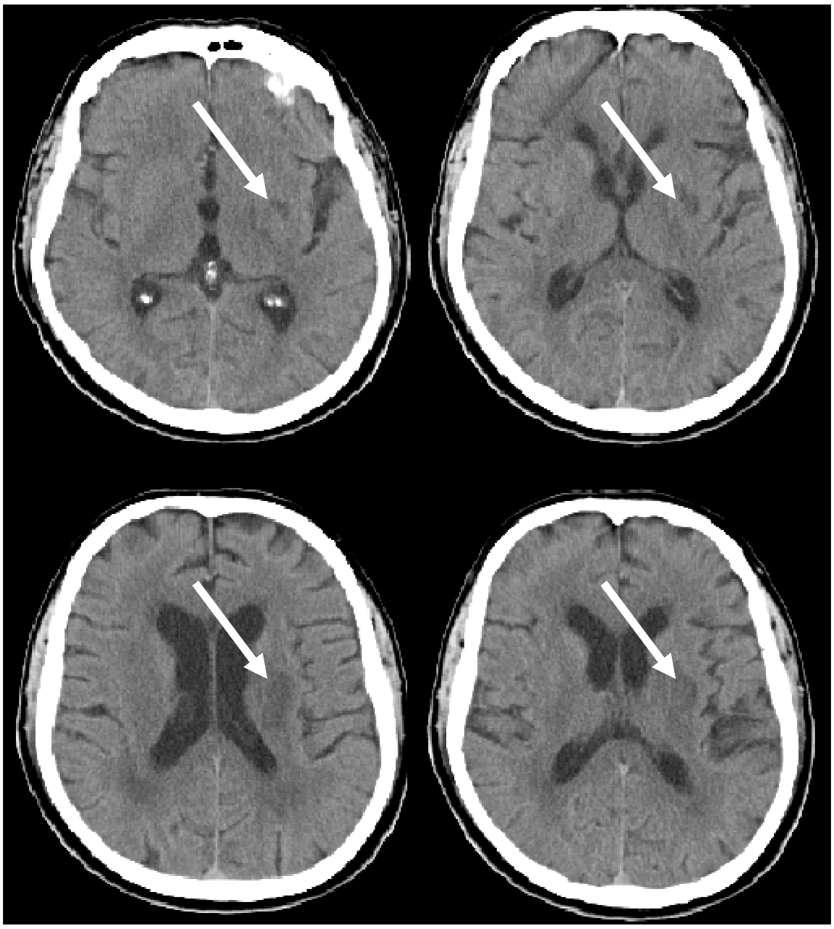

Figure 2.1: OTM’s CT scan. Four images are presented in radiological convention (left hemisphere on the right). The axial sections are organized in a clockwise fashion. They show that the lesion involves left basal ganglia, the corona radiata, and the surrounding white matter (see main text for details).

2.2.1. Neuropsychological assessment

The patient was given a general neuropsychological assessment in September 2005 (see table 2.1.). He obtained similar values of WAIS-R (Wechsler, 1981) Verbal and Performance IQs. OTM's Verbal IQ was in line to those obtained by previous dynamic aphasic patients (Costello & Warrington, 1989; Robinson et al., 1998; Robinson et al., 2005) while his Performance IQ was in line to that of patient ANG (Robinson et al., 1998) and close to that of another case (Costello & Warrington, 1989) but considerably lower than that of CH (Robinson et al., 2005). One of the most striking results on the WAIS-R was OTM's very poor performance on the Picture Arrangement task. That OTM's anterograde memory may be mildly impaired is suggested by his performance on a short story recall (Novelli et al., 1986). As far as attentional functions were concerned, selective attention was severely impaired (Attentive Matrices, Spinnler & Tognoni, 1987). Interestingly, OTM made many perseverations in this test as the targets for the first and second matrix were frequently incorrectly selected in the third matrix.

Table 2.1

Patient OTM’s results on the general neuropsychological assessment.

TESTS	**Raw Scores**	**Normative data (Mean ± SD)**	**Cut offs**
WAIS-R:			
Verbal IQ	83		
Digit span*	7		
Vocabulary*	6		
Arithmetic*	8		
Similarities*	9		
Performance IQ	85		
Picture Completion*	9		
Picture arrangement*	5		
Block design*	8		
Object assembly*	8		
TIB [a]	QI = 101		
LANGUAGE:			
Aachner Aphasiae Test (AAT)[b]			
Token test (num. errors)	**13/50**	2.0 ± 2.3	
Repetition	**129/150**	147 ± 3.2	
Comprehension	103/120	110 ± 8.4	
Reading/Writing	80/90	87.2 ± 4	
Naming	108/120	114 ± 4.3	
Non Literal Language Comprehension[c]:			
- Metaphoric Expression	24/40		average*
- Idiomatic Expression	22/40		average*
MEMORY			
Spatial Span – Corsi test[d]	5	4.67 ± 0.95	≤3.75
Short story recall [e]	**7**	12.41 ± 3.28	≤ 8
Recognition memory test:			
Short Recognition Memory Test for Faces [f]	24/25	22.8 ± 1.9	
Recognition Memory Test for Words [g]	41/50	40.9 ± 4.8	
LOGICAL FUNCTIONS:			
Coloured Progressive Matrices - CPM [h]	25/36	27.22 ± 5.59	≤18.96
ATTENTION:			
Attentive Matrices [i]	**24/60**	48.36 ± 8.55	≤ 31
VISUAL PROCESSING:			
Screening test (VOSP) [l]	19/20	19.92 ± 0.33	≤ 15
Object Decision (VOSP)	17/20	17.7 ± 1.9	≤ 14
IDEOMOTOR APRAXIA (IMA):		No IMA > 62	
AIM test [m]	64/72	Borderline 53 - 62	< 53

Notes. The **bold** character indicates pathological scores. *= age-scaled scores; [a] Brief Intelligence Test, Sartori, Colombo, Vallar, Rusconi, & Pinarello, (1995); [b]Luzzatti, Willmes, & De Bleser, (1996); [c] Papagno et al., (1995); [d] Spinnler & Tognoni, (1987); [e] Novelli et al., (1986); [f] Camden Memory test, Warrington, (1996); [g] Warrington, (1984); [h] Carlesimo, Caltagirone, & Gainotti (1996); [I] Spinnler & Tognoni, (1987); [l]Warrington & James, (1991); [m] De Renzi, Motti, & Nichelli (1980).

2.2.2. Frontal executive functions

The patient was administered a series of tests sensitive to frontal executive dysfunction (see table 2.2.) that revealed severe deficits on this cognitive domain. He was tested on the Modified Card Sorting test (MCST, Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2004) using the administration procedure described by Nelson (1976). The MCST is a shortened version of the original Wisconsin Card Sorting Test (WCST), in which only 48 items are employed, with ambiguous stimuli that can be classified according to more than one category excluded. OTM performed very poorly on this test completing only two categories; he was also highly perseverative (14 errors were perseveration). OTM was also impaired on both phonemic (Carlesimo et al., 1996) and semantic verbal fluency tests (Spinnler & Tognoni, 1987).

OTM was also administered a card version of the Stroop test (Barbarotto et al., 1998). It consisted of 3 cards, each with 100 stimuli, organized in 10 columns and 10 rows. The patient was requested to scan each card from the left and having to give the appropriate responses as quickly as possible. The stimuli on the first card were five colour words (red, blue, green, brown, and violet) printed in congruent colours and OTM was asked to read all words aloud. The second card consisted of squares in the five colours and he was asked to name the colours of the squares. Finally, the third card involved the names of the 5 colours printed in a conflicting ink colour. OTM had to name the ink colour of the printed words. The patient promptly and correctly read the words of the first card and reported the colours of the squares of the second card. For the third card the number of correct responses in the fixed time of 30 s was recorded following Barbarotto and colleagues' procedure (1998). OTM performed very poorly on this card being able to name correctly the colour of only 2 words in the first 30 seconds. In contrast to his poor performance on the Stroop, MCST, and fluency tests, OTM performed at average level in the standard version of the Brixton test (Burgess & Shallice, 1996), and he passed both the Cognitive Estimates Test and the Trail Making Test (see table 2.2.).

Table 2.2

Patient OTM's results on frontal executive tests

TESTS	**Raw Scores**	**Normative data (Mean ± SD)**	**Cut offs**
EXECUTIVE FUNCTIONS:			
WCST- Nelson's modified version [a]			
- n. of Categories	**2/6**	Normal range: 4 – 6	≤ 3
- n. of Perseverative Errors	**14**	Normal range: 3 – 0	≥ 6. 40
Stroop Test [b]	**Failed**		
Brixton Test [c]			
- Standard (num of correct)	36/55 SS = 5	SS = 5 moderate aver.	
Cognitive Estimates [d]	Pass		
- Absolute error score	15	10.81± 3.71	18
- Total bizarreness	2	1.42 ±1.31	4
Trail Making Test [e]:			
- Trail A	Time = 45"	67.26 ± 28.69	≥ 94
- Trail B	Time = 210"	167.54 ± 97.41	≥283
Verbal Fuency (FAS) [f]	**10**	30.77 ± 11.09	≤ 17.35
Semantic Verbal Fluency [g]			
- Animals	11		
- Fruits	5		
- Colors	8		
- Cities	9		
Total score	**33/4 = 8.25**	16.76 ± 4. 38	≤ 7.25

Notes. The **bold** character indicates pathological scores. [a] Caffarra et al., (2004) [b] Barbarotto et al., (1998); [c] Burgess & Shallice, (1996); [d] Della Sala, MacPherson, Phillips, Sacco, & Spinnler (2003) (original version by Shallice & Evans, 1978); [e] Giovagnoli et al., (1996); [f] Carlesimo et al., (1996); [g] Spinnler & Tognoni, (1987), a raw score of 8.25 indicates a mild impairment on this test.

2.2.3. Language baseline

OTM was assessed on a wide range of language tests from the Italian version of the Aachener Aphasie Test (AAT, Luzzatti et al., 1996; see table 2.1). He showed a mild deficit on the Token Test and in repetition of sentences. For the Token Test, OTM's understanding of simple verbal commands was intact. Errors (13/50) were made only in the most difficult subtests of the test, when he was required to retain two characteristics of the tokens at a time (i.e. shape and colour, colour and size). Errors (21/150) in repetition of sentences were characterized by omissions of one or two words when asked to repeat long sentences. Repetition of words was within normal limits. On the comprehension subtests his performance was within the normal range. In addition his reading, writing and naming skills were normal, as well as comprehension of metaphors and idioms (Papagno et al., 1995; see table 2.1.).

Speech production

OTM' spontaneous speech was greatly reduced; he could produce only short phrases of 3-4 words. Family members claimed he tended not to speak at home, while before the stroke he had been very loquacious. He showed mild disprosodia and mild articulatory problems. When asked to speak, he was very often unable to communicate what he appeared to want to say, and he usually stopped in the middle of a sentence. When asked to describe something (i.e. what he remembered of his first stroke) his answers were characterized by many repetitions, interruptions and circumlocutions. For example, when asked to describe how he felt after his stroke he produced the following: *meglio…ma più di tanto non so come parlar…non so come parlar…parlo un pò con mia moglie…ma più di tanto…(50 s)(I feel better…but I do not know how to speak….I do not know how to speak…I speak a little with my wife…but not so much…)*

OTM' speech was also analysed using tasks that elicited speech from pictorial stimuli. In order to obtain a spontaneous speech sample we asked OTM to generate a story from three simple pictures taken from the BADA (Battery for the Assessment of Aphasic Deficits, Miceli, Laudanna, Burani, & Capasso, 1994). He was given 1 min to produce a story for each picture. OTM was also asked to talk about both his job when he worked and the city where he lives. One minute was again given for each topic. Five Italian control subjects matched to OTM for age, education, and gender carried out the same tasks (see table 2.3. for their performance and for comparison with OTM). The modified t-test of Crawford and Garthwaite (2002) was used to contrast the performance of OTM with that of control subjects. OTM produced significantly less words than controls when he was required to speak about his job and his city, whereas there was only a trend towards a difference between OTM and controls on the story generation task. Globally OTM produced less words (word/minute ratio; see table 2.3) than normal subjects but he was close to the rate of word production of other dynamic aphasic patients. OTM always began the story generation task by providing good descriptions of the pictures he saw. Only rarely did he attempt to construct a story as required. By contrast, controls provided less detailed descriptions but tried to produce a story for each single picture. This difference in fulfilling task requirement could be the reason why OTM did not differ from controls in the story generation task while doing so when asked to describe, for example, his city. In this latter task, stimuli (i.e. describe your city) provide less constrains for verbal production relative to pictures which act as cues for production in the story generation task.

Table 2.3

Speech rate of patient OTM, 5 matched controls, and 4 other dynamic aphasic patients

	OTM	Controls	t (4)	ANG [a]	MP [b]	CH [c]	KAS [d]
Story Generation (3 X 1min)[#]	50	130.2 ± 45.15	-1.62				
Event Description (2 X 1 min)[#]	39	169 ± 47.5	**-2.5**				
Speech Rate (words per min)	17.8	59.8 ± 17.63	**-2.17**	29.2	< 20	12.0	23.0

Notes. The total number of words produced are reported in each cell. The Standard Deviation for controls is also reported. [#] See text for details on these tests. The **Bold** character indicates significant differences between controls and OTM. [a] Robinson et al. (1998); [b]Raymer et al. (2002); [c] Robinson et al. (2005); [d] Robinson et al. (2006).

Summary

In sum, OTM showed impairments in intellectual, language, and executive functions as well as having problems in verbal memory and selective attention. Within the language domain OTM had a dissociation between dramatically reduced spontaneous propositional speech and either preserved or only mildly impaired (i.e. Token Test and repetition of sentences) use of language in comprehension and naming skills. The diagnosis derived from the AAT (Luzzatti et al., 1996) was that OTM was not affected by aphasic disturbances. However, his dysphasic impairment falls within the classification of pure dynamic aphasia (Luria, 1973; Robinson et al., 2005, 2006).

The next experimental series of tests was designed to investigate OTM's language output disorder.

2.3. Word and sentence level generation tasks

The aim of this experimental series of tests was to pinpoint the nature of OTM's word and sentence level generation impairment. Most of the tests were based on those used by Robinson et al. (1998, 2005 and 2006). In addition other tests based on those of Costello and Warrington (1989), and Warren et al. (2003) were used. For comparison purposes OTM's performance in each test was contrasted with that obtained from another sample of five age, gender, and education matched controls. As reported above, the modified t-test of Crawford and Garthwaite (2002) was used to make comparisons where needed. Where necessary, reaction times were calculated from a tape recording. Reaction times were defined as the time between the end of the stimulus and the onset of a response.

Generation of sentences from single common words and single proper nouns (Robinson et al., 1998)

Single common words and single proper nouns were given one at time to OTM who was asked to produce a whole sentence incorporating the target word. Both the responses of patient OTM and those of control subjects are reported in table 2.4. (the performance of patients ANG, CH and KAS, of Robinson et al., 1998; 2005; and 2006 respectively, is also included in the table).

Remarkably, OTM produced sentences with the same structure for seven of the twelve common words and for eight of the twelve proper nouns. Despite his tendency to produce sentences with the same structure, the sentences OTM generated were always grammatical and meaningful. Hence, he globally produced 8/12 and 10/12 correct sentences from, respectively, common words and proper nouns. Control subjects performed at ceiling in this task. OTM’s performance did not differ from that of controls on either kind of stimuli ($p > 0.09$ for both comparisons –common words, proper nouns). Moreover he did not show any significant difference across the two task conditions (OTM common words vs. OTM proper nouns, χ^2 (1) = 0.22, P = 0.64).

With common words he provided an explanation of function (e.g. *“Il tavolo serve per mangiare”* –“The table is needed for eating”- for the word “*Tavolo” –*“Table”-*)*. Two sentences of this group were correct but OTM initiated them only after very long pauses (>13 sec), while he did not produce anything at all when given two other words. With proper nouns OTM used the expressions “*bellissimo” and “bravissimo”* (“very beautiful and very good”) (e.g. *“Pippo Baudo”* prompted *“Pippo Baudo e’ un bravissimo conduttore” –*“Pippo Baudo is a very good showman”-). For two of these stimuli he did not make any attempt to produce a sentence.

Clearly, OTM did not have problems in generating a response in this task; however he appeared to use a compensatory strategy in coping with task demands (*explain function* for common words and *report a description* for proper nouns). Thus when he was asked to vary the structure of the sentences he was producing, he complained that the task was too difficult and that he did not have any other word in mind. Moreover, OTM may have perseverated on this test, as have other patients with subcortical lesions when tested on similar tasks (Esmonde, Giles, Xuereb, & Hodges 1996; see also patient MP, Raymer et al., 2002, for strategy use). OTM performed this task differently by ANG and CH who had more difficulties in generating sentences from common words than from proper nouns. As also stated in Robinson et al. (2006), proper nouns are associated with a dominant response or with few verbal response options, while common nouns tend to elicit many response options.

Generation of a sentence from word pairs with strong and weak associations (Robinson et al., 1998)

The stimuli used in this task were the same of those of Robinson et al. (1998). They consisted of strongly associated word pairs (e.g. *"giraffa-collo"*, "giraffe-neck") and weakly associated word pairs (e.g. *"bambino-dolce"*, "baby-sweet"). OTM was asked to produce a sentence incorporating both words of the pair. As for patient ANG, OTM had more difficulties in producing sentences from weakly associated word pairs than from strongly associated ones (χ^2 (1) = 5.62, P < .02) (see table 2.4.). Control subjects had no difficulty with this task.

Generation of single words to complete sentences with high and low response predictability (Robinson et al., 1998)

This task consisted of 20 sentence frames to be completed with a single word where there were few response options (e.g. "The boy sent the letter without the.." with "stamp" being the selected response for 98% of the subjects; Bloom & Fischler, 1980; "*Il ragazzo spedì la lettera senza..*" *"francobollo"*, is the Italian version) and also 20 sentences which had many response options *(*e.g. "The policeman had never seen a man so.." with "drunk" being the most often selected response, 18% of the subjects; *"La polizia non aveva mai visto un uomo così.."*, is the Italian version). The sentences given to the patient were an Italian translation of either the corresponding sentences used in a previous study with a dynamic aphasic patient (Robinson et al., 1998) or of the sentences of Bloom and Fischler (1980).

OTM produced appropriate responses (in less than two seconds on average) for almost all the sentences with high response predictability (with low competition in the response set). By contrast his performance was significantly impaired on the low response predictability sentences (with high competition in the response set) (χ^2 (1) = 8.02, P < .006, see table 2.4.). Control subjects performed at ceiling in this task.

Generation of phrases to complete sentences with high and low response predictability (Robinson et al., 1998)

This task consisted of sentence frames, based on those of Robinson et al., (1998), to be completed by the addition of a whole phrase. Twenty had few plausible verbal response options for their completion (e.g. “The hairdresser moved next to the lady with her scissors and…”; *“La parruchiera ando’ verso la donna con le forbici e..”*, is the Italian version) while 20 sentences had many plausible verbal response options for their completion (e.g. “The man sat in his chair and..” ; *“L’uomo si sedette sulla sua poltrona e…”* is the Italian version). Each sentence was read to the patient. As for patients ANG and CH, OTM produced significantly more phrases in completing sentences with a highly predictable response (the mean voice onset time for the correct responses was 2.8 seconds) than in case of sentences with low predictability of the response (mean voice onset time 3.2 seconds; χ^2 (1) = 4.10, $P < .05$) (see table 2.4.). Controls perform at ceiling on this task.

Elaboration of nuclear sentences (Warren et al. 2003)

OTM was presented with 10 complete sentences and asked to produce a second sentence developing the theme of the first. OTM did not provide any answer for 3 out of 10 sentences. For five sentences OTM provided only a completion without generating a separate sentence (e.g. for the sentence: *“La ragazza ascoltava la storia..”*, “The lady was listening to the story…”, after more than 15 sec he said *“del suo ragazzo”*, “of her boyfriend”). For the remaining two sentences OTM produced a correct response. Controls had no difficulty with this task.

Sentence construction task (Costello & Warrington, 1989)

Dynamic aphasia can also be present in the context of concomitant syntactical or verbal planning impairments. OTM was provided with 10 sentences of four to eight words in length which had to be rearranged. Single words were printed on separate pieces of paper and had to be reorganized to construct a meaningful sentence. OTM performed well in this task (9/10). His only hesitation concerned one of the two seven-word sentences. He rearranged the target sentence: *“Ieri Luca ha rotto la sua macchina nuova”* (“Yesterday Luca broke his new car”) as *“Ieri Luca ha rotto sua la macchina nuova”*. Insofar as this task is one of verbal planning (Costello & Warrington, 1989) this ability was shown to be spared in OTM. Controls also had no problem in this task (see table 2.4.).

Generation of a sentence given a pictorial scene (Robinson et al., 1998)

As shown in table 2.4 previous studies with dynamic aphasics had found that patients were able to provide simple descriptions of pictorial scenes. In this test OTM was given a series of pictures taken from the BADA (Miceli et al., 1994) and was told to create a sentence that described the content of the picture. The patient was able to do this for all the pictures he saw (10/10). Controls also performed errorlessly in this task.

Generation of a sentence from a single picture (Robinson et al., 1998)

Patient ANG (Robinson et al., 1998) was impaired when asked to produce whole sentences (i.e. more than a simple description) that incorporated the meaning of single pictures with which he was presented. OTM was presented with twenty single pictures selected from the BADA battery (Miceli et al., 1994) and required to produce a whole sentence incorporating the meaning of the picture, but not to simply describe it (see table 2.4.). Pictures were divided in two groups: 10 were of objects whereas 10 were of either persons or animals carrying out an action. The pictures from the two groups were presented at two different times. Like patient ANG, OTM's performance was seriously impaired in this test (only 2 out of 20 sentences were correct). In most cases, OTM merely produced a description of the picture rather than generating a whole sentence as required. Controls performed at ceiling.

Table 2.4

Word and sentence generation tasks: summary of correct responses on each task of patients OTM, ANG, CH, KAS and control subjects

Word and sentence level generation tests	Number correct				
	OTM	ANG [a]	CH [b]	KAS [c]	Controls
Generation of sentences from					
a. Common words	8/12	11/28	10/30	14/15	12/12
b. Proper nouns	10/12	26/28	22/30	15/15	12/12
Generation of sentences from					
a. Pairs with strong association	23/30*	22/30	NT	15/15	30/30**
b. Pairs with weak association	13/30	4/30	NT	15/15	30/30**
Generation of single words to complete sentences					
a. High predictability	19/20*	NT	NT	NT	20/20
b. Low predictability	10/20	NT	NT	NT	20/20**
Generation of phrases to complete sentences					
a. High predictability	17/20*	9/12	19/22	10/10	20/20
b. Low predictability	10/20	3/12	11/22	10/10	20/20**
Elaboration of nuclear sentences	2/10	3/20	NT	5/5	10/10**
Sentence construction task	9/10	14/15	9/10	8/10	10/10
Generation of a sentence given a pictorial scene	10/10	34/34	20/20	15/15	10/10
Generation of a sentence from a single picture	2/20	0/6	NT	9/10	20/20**

Notes. * Indicates significant differences (p < .05) across the two conditions of the relative test for patient OTM. ** Indicates significant differences (p < .05) between OTM and control subjects in the test. NT = not tested. An arbitrary cut-off of 10 seconds was adopted for all the tests reported in this section; responses generated after this time were excluded by the analyses. [a] Robinson et al. (1998) ; [b] Robinson et al. (2005) ; [c] Robinson et al. (2006).

Summary and conclusions from the word and sentence generation tasks

The word and sentence level generation tests showed that OTM has difficulties in generating words, sentences and phrases. However, in certain cases he was able to produce plausible words and phrases. OTM was particularly impaired when stimuli activated many response options (phrases and words low in response predictability, word pairs weak in association). By contrast he generally performed much better with stimuli that strongly constrained a response (phrases and words high in response predictability, word pairs strong in association). In these respects OTM’s performance resembled that of the dynamic aphasic patients ANG and CH (Robinson et al., 1998, 2005). The results from this series of tests showed that OTM had problems in generating verbal messages in condition of high competition between multiple response options. However, OTM behaved differently from ANG or CH in some ways. Qualitatively he performed just in the normal range in the generation of sentences from proper nouns and common words. Nevertheless, as reported above, he appeared to use a compensatory strategy in this task.

Gold et al. (1997) reported the case of patient CO who also became dynamic aphasic following a BG lesion, namely a bilateral striatocapsular infarction. CO also presented with signs of executive dysfunction. CO performed poorly on a semantic categorization task and on a procedural discourse test. The authors argued that he suffered from an impairment of concept formation as well as from defective semantic strategy formation. They held that the latter problem was confirmed by the difficulty the patient had in sorting items from very closely related categories by contrast with his intact performance in sorting items from more distantly related categories. Gold et al. (1997) suggested that CO's deficits might reflect a more general impairment in the ability to organize knowledge in a hierarchical fashion. The following section aims to assess whether OTM's problems in producing verbal responses in situations of high competition may be due to deficits in concept generation and in semantic strategy formation.

2.4. Routine activities description and semantic strategy formation

Procedural discourse task (Gold et al., 1997)

In Gold et al.'s (1997) version of the task the patient had to describe the steps involved in carrying out a series of common actions such as preparing a cup of coffee. The patient performed the task in two conditions. First he described the steps involved in the procedures without any prompting, whereas in the second the experimenter provided the patient with cues such as "the first step is…" etc.

We administered a similar task to OTM but changing some of the required actions to fit with those used by Rumiati, Zanini, Vorano, and Shallice (2001). These authors provided a list of the verbal descriptions of the discrete steps involved in a series of multi-objects-actions (MOT) that they administered to their apraxic patients. They distinguished a total of 47 steps for 10 common tasks with 7 tasks being divisible into 5 discrete steps and 3 tasks into 4 steps. The procedures were: *Preparing orange juice, Making coffee using a coffee pot, Lighting a* *cigarette, Preparing a letter for posting, Pouring water from a bottle, Lighting an electric torch, Hanging a small picture, Lighting a candle, Sharpen a pencil, Peeling a potato.*

OTM was asked to describe the steps he usually goes through in carrying out these actions. He performed as well as normal subjects (n = 5) in this task. OTM gave an average of 3.9 steps for each action while controls gave descriptions formed of 4.3 steps on average with the difference being not significant (t (4) = -0.97; modified t-test, Crawford & Garthwaite, 2002). Given OTM's ability to perform the task he was not administered the sequence cued condition used by Gold et al. (1997).

Semantic categorization task (Gold et al., 1997)

Before assessing OTM's abilities in semantic strategy formation and semantic categorization, we evaluated his ability to access semantic representations. OTM was tested using only the picture section of *The Pyramids and Palm Trees Test* (Howard & Patterson, 1992), a test specifically aimed to assess the integrity of the semantic network. His performance was well within the normal range and almost at ceiling (50/52) indicating that he could recognize the items and retrieve conceptual and semantic information about them.

Given that OTM's ability to access meaning from pictures was intact we gave him a semantic categorization task. We used the procedure developed by Robinson et al. (2005) and the categories these authors employed. They had found that the dynamic aphasic patient CH was unimpaired in this task. OTM was required to sort items into two categories. A set of 80 words and a set of 80 pictures were chosen. Each of the two groups of stimuli formed 16 categories, each consisting of five highly associated items. Pairs of categories were used with their degree of association being either distant or close. OTM was given 10 cards at the same time and was required to sort the pictures or the words into two groups of five each. In one condition the names of the two categories were given in advance to the patient (cued condition) and in another the names of the categories were not given (uncued condition).

OTM's performance on this task is reported in table 2.5 together with CH's performance (Robinson et al., 2005) and that of four control subjects who were administered the task. OTM's performance on the task was good and similar to that of CH (Robinson et al., 2005) and of normal controls. OTM was only somewhat slower than controls in the uncued condition of the closely related word pairs category (t (3) = 2.88, $p < 0.05$).

Table 2.5

Semantic categorization task

	PICTURES				WORDS			
	Close		Distant		Close		Distant	
Condition	N. Correct	Mean RT	N. Correct	Mean RT	N. Correct	Mean RT	N. Correct	Mean RT
				CUED				
OTM	40/40	12	40/40	10	38/40	23	40/40	18
CH [a]	39/40	28.3	40/40	25.5	40/40	18.8	40/40	20
Controls	40/40	13 (2.2)	40/40	11.5 (1.9)	39/40	15 (3.9)	40/40	14.2 (4.3)
				UNCUED				
OTM	38/40	25	40/40	13	35/40	44	40/40	18
CH [a]	38/40	47	40/40	28.3	37/40	34.8	40/40	19.3
Controls	38.2/40	26.2 (7.1)	40/40	16 (7.7)	37/40	22.75 (6.6)	40/40	16.5 (3.8)

Notes. Response times are expressed in seconds. Standard Deviations for controls are shown in parentheses. [a] Robinson et al. (2005).

Summary and conclusions from the procedural discourse and the semantic categorization tasks

Given OTM’s intact performance on the procedural discourse task, an explanation of his deficits in terms of impaired generation of concepts can be ruled out. OTM was able to retrieve information in order to generate phrases for describing well learned actions. OTM performed very differently from Gold et al.’s patient in this test. The results of the semantic categorization task showed that OTM did not have a semantic strategy formation deficit of the kind proposed by Gold et al. (1997) to account for the difficulty their patient showed on the task. In this respect the findings on OTM are similar to those on patient CH (Robinson et al., 2005).

2.5. Random number generation task

In this task OTM’s ability to generate numbers was investigated. As discussed in Robinson et al. (2005; see also Cappelletti, Butterworth, & Kopelman, 2001), numbers are a special category which can dissociate from other linguistic categories. In the Introduction we have also reported evidence showing that patients with BG pathology may be unable to generate numbers in random order (e.g. Brown et al., 1998). On the other hand, dynamic aphasic patient CH (Robinson et al., 2005) had performed in the normal range on this task. The task that we used consisted of three conditions differing in the size of the response set. In the first part of the task OTM was asked to generate numbers within the set 1-9 in a random order. In order to illustrate the concept of randomness, both the control subjects and patient OTM were given the analogy of picking a number out of a hat, reading it aloud, putting it back, and then picking another. The number set 1-9 was followed by two conditions in which the response set was more restricted, OTM having to generate numbers from the sets 1-4 and 1-2. Each condition involved 100 numbers. OTM had to generate a number in time with a tone occurring once every 3 seconds, as used by Robinson et al. (2005). The percentages of number repetitions (e.g. the series 2-2 was scored as 1), descending series (e.g. 4-3, scored as 1) and ascending series (e.g. 3-4, scored as 1; or 3-4-5, scored as 2) were calculated.

OTM’s performance is reported in table 2.6 along with that of control subjects. For comparison purposes performance of patient CH is reported as well. OTM performed significantly differently from control subjects in each kind of response for the 1-2 number set. In the number set 1-4 OTM produced significantly more descending series than did the controls. In the largest number set (1-9) OTM produced more responses that were part of ascending series than control subjects.

Summary from the random number generation task

The random number generation task showed that OTM differed from normal controls particularly in the length of ascending and descending series he generated. This behavior was not related to the size of the response set since differences between OTM and controls were present in all conditions of the task. Excessive use of ascending and descending sequences of numbers have also been reported in the context of TMS involving the left dorsolateral prefrontal cortex (Jahanshahi et al., 1998; see also Brown et al., 1998) and, as noted also by Robinson et al. (2005), this may indicate an associated deficit for OTM.

Table 2.6

Random Number Generation task

Number Generation task	Chance % Responses	OTM % Responses	Controls % Responses	t(4)	CH[a] % Responses
			Number set (1-2)		
Repeats	48	36.5	51 (4.33)	***-3.05**	48
Ascending series	25	32	25 (2.77)	***2.31**	28
Descending series	25	31.2	24 (1.2)	***5.47**	23
			Number set (1-4)		
Repeats	25	0	11.2 (7.72)	-1.32	30
Ascending series	18.75	33.7	22.2 (5.54)	1.89	21
Descending series	18.75	33.7	21 (4.63)	***2.50**	25
			Number set (1-9)		
Repeats	11.1	0	2 (1.9)	-0.96	2.5
Ascending series	9.9	20.4	8 (4.78)	***2.36**	24
Descending series	9.9	23.4	17 (5.16)	1.13	13.5

Notes. *Indicates significant t values ($p < 0.05$) for comparison between OTM and controls. Responses are reported as percentage. Standard Deviations for controls are shown in parentheses. [a] Robinson et al. (2005).

2.6. Nonverbal generation tasks

Robinson et al. (2005) described the dynamic aphasic patient CH who was found to have largely preserved abilities to give non-verbal responses, performing as well as normal controls in some non-verbal generation tasks. This was taken as evidence that CH’s dynamic aphasia did not extend beyond the domain of language. The next session aims to asses whether

OTM's generation deficit too did not extend to cognitive domains other than language. Two of the tests used by Robinson et al. (2005) were chosen: figural fluency (Five-Points test), and motor movement generation.

Five-Points test: a figural fluency test

The five points test is a measure of non-verbal figural fluency. A subject is presented with a sheet of paper that consists of 40 five-dot matrices arranged in 8 rows and 5 columns. The subject is required to connect the dots in as many different ways as possible. Lee, Strauss, Loring, McCloskey, and Haworth (1997) found that patients with frontal lobe dysfunction made many more perseverative errors than nonfrontal neurological and psychiatric patients. Frontal lobe patients produced about 25 designs with 27% perseverations on the 3-minute version which we used. By contrast, the dynamic aphasic patient CH (Robinson et al., 2005) drew 20 different designs without making any perseveration.

OTM did not significantly differ from control subjects in the total number of designs produced. OTM produced 15 designs while control subjects drew a mean of 16.6 designs on average ($t(4) = -0.39$; modified t-test, Crawford & Garthwaite, 2002). However, considering only the number of novel designs produced, OTM performed clearly worse than normal controls (6 vs. 13.8 respectively, $t(4) = -6.5$; $p < 0.001$). In fact OTM made 9 (60%) perseverative errors while controls made only 2.8 (16%) perseverations on average, the difference being highly significant ($t(4) = 5.16$; $p < 0.005$, modified t-test, Crawford & Garthwaite, 2002). OTM's performance on this test was extremely poor showing a clear impairment of perseveration in figural fluency.

Motor movement generation

In this test OTM was provided with a joystick which could be moved in four directions: right, left, up and down. OTM was requested to select a movement using the joystick whenever he heard a sound that occurred once each 3 seconds. He was told that the movements did not have to reproduce a schema or a pattern. Owing to his right hemiplegia OTM moved the joystick with his left hand. The task was divided into three conditions according to the number of movement options he could select. In the first two conditions OTM could select between two movement options, either Left (L) and Right (R), or Up (U) and Down (D); in the third condition there were four movement options: U, D, L, R. As in Robinson et al.'s (2005) study, each condition lasted 4 minutes. OTM was familiarized with the task by performing a baseline condition of 2 minutes in which he had to move the joystick in one direction (U) in time with the sound (once each 3 seconds). The percentages of repeated responses (e.g. L-L) and opposite responses (e.g. L-R) were calculated in order to have measures of fixed or random responses. Table 2.7 reports OTM's results together with those of CH and control subjects. No t values (modified t-test, df = 4; Crawford & Garthwaite, 2002) reached significance when OTM's performance was compared with that of control subjects.

Table 2.7

Motor movement generation task

Motor movement Generation Task	Chance	OTM	Controls		CH[a]
	% Responses	% Responses	% Responses	t(4)	% Responses
			Two Options		
Left-Right					
Repeats	50	40	48.6 (6.54)	-1.19	42.9
Opposites	50	60	51.4 (6.54)	1.19	57.1
			Two Options		
Up-Down					
Repeats	50	51.3	52 (14)	-0.04	52
Opposites	50	48.7	48 (13.7)	0.04	48
			Four Options		
Up-Down-Left-Right					
Repeats	25	1.4	17 (8.45)	-1.68	38.8
Opposites	25	36.6	33 (4.06)	0.80	23.8
Other	50	62	50 (11.55)	0.94	37.4

Notes. Responses are reported as percentage. Standard Deviations for controls are shown in parentheses. [a] Robinson et al. (2005).

Summary and Conclusions from the non-verbal generation tasks

OTM's performance on the non-verbal generation tasks varied across tasks. OTM has normal performance in the motor movement generation task while he was impaired in the figural fluency test. Although OTM did not differ from normal controls in the number of total responses generated in this test, he produced a small number of novel designs and he made many more perseverations than controls.

2.7. Discussion

OTM presented with abnormally reduced propositional language following an ischemic stroke to the left basal ganglia. His language production was characterized by reduced fluency particularly in situations requiring more than a simple description of the stimulus. OTM's reduced spoken language was not connected to general deficits in reading, repetition, naming or comprehension, as these skills were either preserved or only mildly impaired. Our patient could only produce short phrases of 3-4 words and exhibited mild disprosodia and mild articulatory problems as well. Globally, this pattern of deficits is consistent with dynamic aphasia (Luria, 1973). Indeed, a quantitative evaluation of his speech rate showed that this was similar to those of other patients reported with dynamic aphasia. In addition to his language output disorder OTM presented with signs of executive dysfunction performing poorly in the Modified Card Sorting Task, phonemic and semantic verbal fluency and in the Stroop test.

A series of tasks were administered aimed at investigating OTM's language output disorder. Results from the word and sentence level generation tests showed that OTM had great difficulties when required to produce phrases and words; his problems became evident when stimuli did not suggest a dominant response. In a similar fashion to patient ANG (Robinson et al., 1998), OTM had more difficulties in producing sentences from word pairs with weak association between them than from strongly associated word pairs and had also many more problems in completing low predictability sentences, either with phrases or words, than high predictability ones. Moreover, like ANG (Robinson et al., 1998) and CH (Robinson et al., 2005) but differently from ROH (Costello & Warrington, 1989), OTM did not show any problem in the sentence construction task. Tests of speech elicitation from pictures (generation of a sentence given a pictorial scene and from a single picture) produced similar results to those obtained in other dynamic aphasic patients (Robinson et al, 1998, 2005); indeed OTM was severely impaired in producing sentences from single pictures whereas he could give a simple description of them.

We also assessed whether OTM suffered from the kind of deficits described by Gold et al.'s (1997) in their dynamic aphasic patient CO who also had a basal ganglia infarction. These authors proposed that their patient suffered from deficits in semantic strategy formation and concept generation, being impaired in both tasks of semantic categorization and procedural discourse. OTM's performance in the latter task showed that he could correctly describe routine activities, and he could generate concepts and combine them in sequences. OTM also performed almost errorless in the semantic categorization task as done by patient CH (Robinson et al., 2005). As discussed by Robinson et al. (2005), the fact that CH and OTM performed normally in the semantic categorization test indicates that they do not have a primary deficit in semantic strategy formation.

OTM's abilities to generate numbers and non-verbal responses were also investigated. In a random number generation task he performed differently from control subjects producing more ascending and descending series of numbers. Non-verbal response generation skills were found to be preserved in one task; OTM was within the normal range in the motor movement generation task. His performance on figural fluency was however impaired; the number of novel responses was below the normal range as 9/15 responses were perseverations.

As already shown, several explanations have been proposed for dynamic aphasia. Most of these try to account for the syndrome within the domain of language while others also involve functions other than language. The case of OTM suggests that we can rule out the possibility that his deficits lay in damage to a mechanism forming the linear scheme of a sentence (Luria, 1973) given that he can produce phrases and sentences in some circumstances. Similarly, the possibility of an impairment in verbal planning that Costello and Warrington (1989) considered for their patient (ROH) can be rejected for OTM. In fact he performed almost errorless on the sentence construction test on which ROH had great difficulties.

Results from the word and sentence generation tasks have shown that the number of response options associated with a task (verbal response alternative options) was an important factor helping to give rise to OTM's performance in many of the tasks we used. In a similar fashion to CH (Robinson et al, 2005), OTM was not impaired when a stimulus strongly suggested a response. By contrast, OTM had great difficulties when stimuli activated many response alternatives. As stated in Robinson et al. (2005), a deficit in the selection of verbal responses in propositional speech is likely to be due to defective mechanisms of conceptual preparation (Levelt, 1989; 1999). Lexical concepts have sometimes to be generated in conditions of high competition, namely when many of them are simultaneously activated. These conditions are those that pose the greatest requirements to the conceptual preparation mechanisms particularly when the latter are defective. The empirical evidence collected in this study suggests that OTM, similarly to patients ANG and CH (Robinson et al., 1998, 2005 respectively), suffers from an impairment in verbal response generation in situations of high competition.

However, differently from CH, OTM also had problems in figural fluency and in the random number generation task. OTM made many perseverations in the figural fluency test while he gave increased ascending and descending series of numbers in the random number generation task. A first possibility is that to consider OTM's problems with numbers as due to a deficit of inhibition. Among the processes assumed to be involved in order to perform well on such a task, one consists of inhibiting the most familiar strategy of counting upwards or downwards in ones which, in the terminology of the SAS model, is the strongest schema in the contention scheduling. Thus, it is possible that OTM's pattern of performance in this task reflects a failure of the SAS to inhibit strong routine schemata (i.e., counting in ones) in favor of switching schemata as is necessary to accomplish the random number generation task (e.g. counting in twos). In fact, as also reported in the Introduction, failure of inhibition has been invoked for explaining deficits on the random number generation task of both patients with BG pathology (Brown et al., 1998) and normal subjects which undergone TMS over the DLPFC (Jahanshahi et al., 1998). DLPFC has been also seen to be involved in other tasks requiring response suppression such as a form of the Stroop test (Alexander et al., 2007). Moreover, the relevance of the circuit involving the DLPFC and the caudate nucleus has been stressed by Gold et al. (1997) in order to account for several of the signs of frontal dysfunction shown by their patient. OTM also showed impairments which correspond to malfunctions of DLPFC (i.e. poor performance on the Stroop test and MCST).

An account in terms of failure of inhibition may also explain OTM's perseverative responses in the figural fluency task; however an alternative possibility exists for explaining his poor performance on this task. Perseverations may reflect a deficit in generating novel content (Robinson et al., 2006). We have shown that OTM was able to produce only 6 different figures relative to controls who generated almost 14 new designs in the figural fluency test. OTM's inability to generate novel content may also be seen to fit with his difficulty in some language tasks. For instance, OTM did not have any problem in producing a response when given common words or proper nouns as a stimulus, however he appeared to perseverate or to use a compensatory strategy in this task (see also his problems in sentence generation from single pictures or elaboration of nuclear sentences in which novel material has to been generated).

In sum, the case of OTM, in a similar fashion to those of the dynamic aphasic patients CO and KAS (Gold et al., 1997; Robinson et al., 2006 respectively; see also Raymer et al., 2002), suggests that subcortical lesions which give rise to dynamic aphasia also lead to deficits in non-verbal domains. OTM’s pattern of performance on both verbal and non-verbal tasks suggests that he suffered from defective generation of novel thoughts as suggested by perseveration and due to either failure of inhibition or defective generation of novel content. Within the domain of language the deficit is particularly present when stimuli activate many competing response options and it may be due to a frontostriatal damage disrupting the left frontal region function of selection in situation of high competition.

As reported in the Introduction, there is a considerable body of neuropsychological and neuroimaging evidence supporting the role of the left inferior frontal gyrus (LIFG) in the process of selection of task-relevant responses in situation of competition (Thompson-Schill et al., 1997; 1998; Barch et al., 2000; Zhang et al., 2004; Persson et al., 2004; 2007; Thompson-Schill & Botvinick, 2006). Moreover, referring back to dynamic aphasia, the literature suggests the involvement of LIFG in this syndrome. A review of dynamic aphasia cases supports, indeed, the role of the LIFG in the emergence of the reduced verbal output which is generally observed in these patients (Costello & Warrington, 1989; Esmonde et al., 1996; Snowden, Griffiths, & Neary, 1996; Raymer et al., 2002; Warren et al., 2003; Robinson et al., 1998; 2005). Admittedly we need to act with caution as far as the interpretation of the CT scan is concerned. As this is not 100% sensitive for ischemic damage, the precise extent of the frontal lesion in OTM cannot be exactly specified. Moreover, the evidence reported in the Introduction about a role of the BG in the suppression of competing alternatives and, more generally, in response selection does not exclude a more direct contribution of these structures to the verbal response generation deficit of OTM. Indeed, there have been reported studies as showing that the BG are involved in the inhibition of irrelevant responses (see chapter 1; see also Dujardin et al., 1999; Rossel et al., 2001; Bouquet et al., 2003; Longworth et al., 2005; Castner et al., 2007) as well as in novel thought generation (Robinson et al., 2006), and, more generally in controlled cognitive processes (Crosson et al., 2003; Copland et al., 2000a, 2000b; Copland, 2003; Redgrave et al., 1999). On the other hand, frontal cortex is also important for response suppression (Stuss et al., 2005; Alexander et al., 2007; Picton et al., 2007; Mostofsky & Simmonds, 2008).

Thus, more generally, it is likely for OTM that an impairment to the BG and the consequent abnormal functioning of subcortical-frontal circuits are important factors in helping to give rise to his deficit of novel thought generation which involves functions both within and beyond the domain of language. A last issue concerns Robinson et al.’s (2006) distinction between different forms of dynamic aphasia. OTM seems to present impairments similar to the second subtype of dynamic aphasia in which both verbal and non-verbal deficits occur following a subcortical damage.

2.8. Testing selection between alternative verbal responses in normal subjects

Aims and empirical background

In the following part of the chapter the ability of selecting responses from among alternative options will be investigated in normal adult subjects, using both similar tasks to those administered to OTM and a stem completion task. To this purpose we run two experimental studies. The only difference between the two experiments lies in the use of a dual-task paradigm in the second one.

In the first experiment, one group of young adults was given two tests commonly used with dynamic aphasic patients (low and high response predictability sentence completion by mean of single words and entire phrases) and a stem completion task. The first two tasks were used in order to confirm the findings on OTM that completion of low response predictability sentences is associated with poorer performance than completion of sentences with high predictability of the response. The performance at ceiling found in older controls on these kinds of tasks (see tests 3 and 4 of table 2.4) suggests that effects are expected to be found only in RT in adult subjects. A stem completion task was also chosen as a task in which performance differences between high and low selection demands conditions (i.e. respectively stems with many possible completions and stems with few possible completions) may be either less evident (than in sentence completion tasks) or even in the opposite direction (i.e. high selection demands performed better than low selection demands) (see Desmond, Gabrieli, & Glover, 1998). The choice of such a task was particularly motivated by the second experiment in which a dual-task paradigm was used.

With regard to sentence completion, relatively few studies have addressed this ability in normal adult subjects. Nevertheless an exception is represented by the PET study of Nathaniel-James and Frith (2002). They presented 6 subjects with a sentence completion task based on the Hayling test (Burgess & Shallice, 1996). Of particular relevance for our aim was the condition A of their study in which subjects had to provide a word to complete each given sentence. The authors varied the level of contextual constraint of the sentences from low to high, so that sentences with low constraint were those that could be completed in many different ways. The authors found that sentences with low constraint activated the left DLPFC more than sentences with high constraint and that the former were completed slower than the latter. Nathaniel-James and Frith considered the DLPFC to operate to specify a set of plausible responses and to bias them for selection.

As far as the stem completion task is concerned, subjects are generally asked to complete a 3-letters stem with a word in this task. Stem completion has been considered to be particularly useful to learn more about the interplay of controlled and automatic processes as some studies have shown that both processes can actually intervene in this task (e.g. Debner & Jacoby, 1994; Meier, Morger, & Graf, 2003). Among the factors that potentially influence the choice of a stem completion, the familiarity of the completion has been proposed to play a crucial role (Ryan, Ostergaard, Norton, & Johnson, 2001). Such a factor is given by word frequency, whereby subjects tend to choose high frequency words more often than low frequency words as completions. A stem completion study that is particularly relevant for our purposes is that of Desmond et al., (1998). In the context of an fMRI design, the authors compared stems with many possible completions (*many* condition; high selection demands) to stems with few possible completions (*few* condition; low selection demands). Desmond and colleagues found that the *many* condition activated the middle frontal gyrus and BG more than the *few* condition; the reverse contrast revealed activation particularly in the right cerebellum. The authors suggested that the middle frontal gyrus and BG supported response selection while cerebellum supported the search for responses which was particularly needed with the *few* stem stimuli. Of importance, there was a trend ($p = .07$) which indicated that subjects were faster in completing stems in the *many* condition relative to the other type of stems. However, a potential problem with this study was given by the fact that words which acted as potential completions of the two stem conditions were not matched for frequency. In fact words that completed the *many* stems were of higher frequency than words that acted as completions of the *few* stems.

In line with previous evidence we assume that word frequency is a crucial factor influencing performance on the stem completion task. Thus, in the present study the words which act as completions in the *many* stem condition are matched for frequency of occurrence to the words which act as completions in the *few* stem condition. Following this procedure we expected not to find any difference in RT across the two task conditions despite their differences in selection demands.

In sum, the rationale of the first experiment consists of testing, in adult subjects, response selection between alternative responses using different kinds of tasks. For the sentence completion tasks we expect to find longer RT in situations of high selection demands (i.e. low response predictability sentences) reflecting the increased processing requirements of these conditions. The use of a stem completion task allows us also to test the hypothesis that in this task, the selection of task-relevant responses is not primarily influenced by selection demands as far as the potential critical factor of word frequency is taken into account.

In the second experiment we test our hypotheses further by asking subjects to perform the same three language tasks (i.e. sentence completion –single word-; sentence completion –entire phrase-; stem completion) while carrying out a concurrent distracting motor procedure which was presented at two levels of difficulty: less demanding and more demanding. In choosing a concurrent task it was necessary to have a task which was both demanding in capacity terms but which could be performed simultaneously with verbal generation in terms of its sensorimotor characteristics. We used a motor task that previous studies have shown to affect performance of some tasks which require PFC (Moscovitch, 1994; Fletcher, Shallice, & Dolan, 1998). As an example, Fletcher et al. (1998) asked subjects to encode different lists of words while executing a sensorimotor task. They found that the more demanding version of the motor task affected the ability to encode specifically the most difficult lists (i.e. the ones which required active organizational processes) by causing an attenuation in left DLPFC activation. These authors suggested that their sensorimotor task produced the analogue of a frontal lobe syndrome in the normal subjects (see also Moscovitch, 1994) and that the source of the interference effect was to be found in the use of attentional resources. In more detail, the higher the processing demands of the memory tasks were, the more pronounced was the interference effect of the motor task.

In our experiment we used the same sensorimotor task of Fletcher and colleagues to test the hypotheses that the more demanding version of the sensorimotor task affects specifically 1) the abilities to select both between competing words and phrases (i.e. performance on the low response predictability sentence completion tasks); 2) but not the high selection demands condition of the stem completion task. These results would show that low response predictability sentences require more processing demands than high response predictability sentences, but also that completion of stems with high selection demands may require similar attentional resources than completion of stems with low selection demands.

2.8.1. First experiment

In this experiment subjects were asked to complete sentences either by adding a single words or an entire phrase and to complete 3-letters stems with a single word. Each task consisted of two conditions which differed in the number of alternatives a response could be chosen from. In both sentence completion tasks there were low response predictability and high response predictability sentences. The former indicate that a sentence can be completed in many different ways while the latter that a sentence can be completed in few different ways. Moreover, there were stems which formed the initial part of many different words (high selection demands condition) and stems which formed the initial part of few different words (low selection demands condition).

Method

Participants

Twelve volunteer participants took part in the experiment. They were 25 years old on average (range = 22-27); 7 were males and 5 females and they were all right-handed. All had normal or corrected-to-normal vision, no history of neurological involvement or auditory impairment.

Apparatus and Materials

The experiment was conducted on a PC with Windows as operative system and E-prime as software for delivering all stimuli. Participants viewed the display at a distance of approximately 60 cm from the centre of the computer screen. They wore headphones over which the auditory stimuli were presented. While subjects listened to each stimulus a fixation cross appeared on the centre of the computer screen. Subjects were required to listen to the sentences or the stems and speak aloud to a microphone when they were ready to produce a response. The latter were tape-recorded. RTs were defined as the time between the end of the stimulus and the onset of a response and represented the dependent variable of the study.

Forty stimuli were used for each task. In both the sentence completion tasks half of the stimuli (20) consisted of low response predictability sentences and the other half of high response predictability sentences. Similarly, in the stem completion task twenty stems formed the low selection demands condition while the others formed the high selection demands condition. For the sentence completion tasks we used the same sentences which we employed in our single case analysis; thus the material for these tasks was in turn similar to that used with patient ANG (e.g. Robinson et al., 1998), and to that of Bloom and Fischler (1980) who provided sentence completion norms on more than 300 English sentences (see third and fourth test of section 2.3. for some examples of sentences used). With regard to the stem completion task we used the *“Veli Dictionary of frequency for spoken Italian”* in order to obtain frequency values of words in spoken Italian language. Twenty stems which had a mean of 21.2 completions (i.e. words; range 14÷29) were selected from the dictionary and served as stems with high selection demands. Twenty stems which had a minor number of completions (mean: 4.1, range 2÷5) were also selected serving as stems with low selection demands. The mean frequencies of usage (obtained, in absolute terms, from the Veli dictionary) of the words which completed the stems of the two conditions were of 198 for the stems with high selection demands and 188 for those with low selection demands, with the difference being not significant (t = .55, p > .05). To give some examples, the stem *"PON.."* was selected as one with low selection demands given that, according to the dictionary, it formed 5 different words (with a mean frequency value of 150). In a similar way, the stem "*ANT..*" was chosen as one with high selection demands being associated to 27 different words in the dictionary (mean frequency value of 148).

Procedure and design

Participants were tested individually in a silent room. They received written instructions explaining both the course of the events and the tasks they were required to perform. Each auditory stimulus was presented to the subjects while a fixation cross appeared on the screen. Subjects had to produce a response within the time limit of 4 sec, after this period a 2sec interval was presented before the next stimulus occurred.

Each tasks consisted of two blocks each consisting in turn of twenty stimuli. Within each block half of the stimuli (10) consisted of either low response predictability sentences or stems with high selection demands, while the other half of the stimuli (10) formed either high response predictability sentences or stems with low selection demands. High and low response predictability (or high and low selection demands) stimuli were presented in two consecutive groups each of 10 stimuli, within each block, and the order of the groups was counterbalanced across the two blocks of each task. The presentation of the 6 blocks of stimuli (2 blocks for each task) occurred in two consecutive series of three blocks each. In both these series of blocks one block for each task was presented. The presentation of the second series of three blocks followed the opposite order of presentation of the first series of blocks (i.e. A-B-C-C-B-A where A, B, and C stand for the three tasks). Similarly to the first block of each task, each second block was formed by half stimuli with low response predictability (i.e. sentences) or high selection demands (i.e. stems) and by half stimuli with high response predictability (i.e. sentences) or low selection demands (i.e. stems). Each subject performed each block of all tasks for a total of 120 stimuli. The order of the tasks varied according to a Latin square design. For instance, the following was the combination of tasks for the first subject: $A_{(1-2)}$ - $B_{(1-2)}$ - $C_{(1-2)}$ - $C_{(2-1)}$ - $B_{(2-1)}$ - $A_{(2-1)}$ in which *1* and *2* stand for first half of stimuli (e.g. low response predictability or high selection demands stimuli) and second half of stimuli (e.g. high response predictability or low selection demands stimuli) respectively.

Data Analysis

The design was a 2 (high and low response predictability or high and low selection demands) x3 (sentence completion –entire phrases- SCP; sentence completion –single words- SCW; stem completion STC) repeated measure design. Mean RTs for each subject and condition were analysed by repeated measure ANOVAs after that a log-transformation guaranteed normality of the distributions (for clarity, RT are however reported in ms in the figures below). For the significant effects, post hoc Bonferroni significant difference comparisons were performed, in order to see which comparisons accounted for the effects. Throughout the thesis an effect was defined as significant if its corresponding α-level was below .05.

Results

As expected, adults performed at ceiling in the tasks (trials without responses represented 1.2 % of the total responses), hence only RT data were analysed. A 2x3 repeated measures ANOVA was performed involving the factors of Condition (high and low) and Task (SCP; SCW; STC). The analysis revealed significant main effects of Task (F (2, 22) = 5.47, p < .02) and Condition (F (1, 11) = 27.19, p < .001), and a significant interaction between the factors (F (2, 22) = 10.84, p < .002) (see Figure 2.2). Post hoc tests were employed, using Bonferroni corrections for multiple comparisons, to explore the global differences between the tasks. These tests showed that SCP do not differ from STC (p = .34), while being significantly slower than SCW (p < 0.002). Moreover a trend is present showing that STC is slower than SCW (p = .083). In view of the interaction we analysed the factor of condition within each task separately. For the SCP task, this analysis showed that low response predictability sentences were slower to be completed than high response predictability ones (F (1, 11) = 28.19, p < 0.001). The same effect occurred between the conditions of the SCW task (F (1, 11) = 21.10, p < 0.002), but no difference was found between stems which differed in selection demands (p = .39).

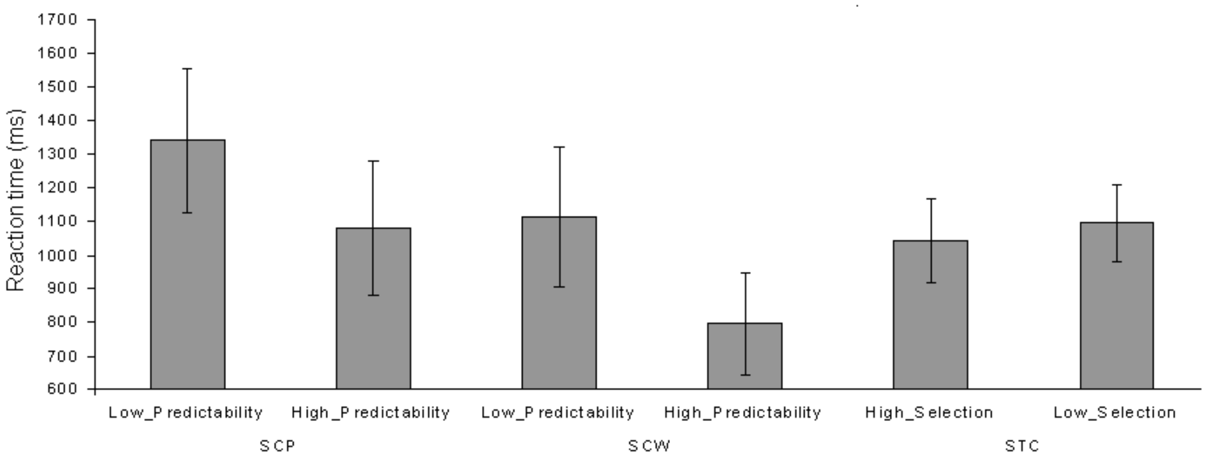

Figure 2.2: Mean reaction times as a function of task (x-axis). Each task is presented in its two conditions. Vertical lines depict standard deviations of the means. SCP stands for Sentence completion by mean of phrase generation; SCW stands for sentence completion by mean of single word generation; STC stands for stem completion.

2.8.2. Second experiment

In experiment 2 the same three language tasks were given to a different group of adult subjects who were asked to complete sentences or stems while simultaneously executing a motor task. As reported above, the latter was presented at two different conditions: there were a less demanding condition (LD) and a more demanding condition (MD). We predict that the latter specifically influences performance (i.e. increased RT) on the low response predictability sentences.

Method

Participants

Twenty-four volunteer participants took part in the experiment. They were 26 years old on average (range = 21-29); 13 were males and 11 females and they were all right-handed. All had normal or corrected-to-normal vision, no history of neurological involvement or auditory impairment.

Apparatus and Materials

The apparatus and stimuli were the same as in the Experiment 1. However, in Experiment 2, subjects listened to the verbal stimuli (either sentences or stems) and responded to these while carrying out a motor task. This consisted of a photograph of a left hand which appeared on the screen for all the duration of the experiment. A red circle of about 2 cm of diameter was superimposed to one of the fingers of the hand (except the thumb) and moved either from the forefinger to the little finger in a predictable way (i.e. passing through the other two fingers), or randomly through the four fingers. The less demanding version of the motor task consisted of predictable movements, while unpredictable sequences were employed in the more demanding version. Subjects were required to press the buttons corresponding to the position of the red circle on a 4-key pad placed under their right hand. Auditory comprehension of stimuli occurred while subjects performed the less demanding version of the motor task. A movement of the red circle from one finger to another occurred once each 900 ms.

Procedures and design

This experiment constituted a 2 x 2 x 3 within subjects factorial design, with the first factor (dual-task) having two levels (LD: less demanding, MD: more demanding), the second factor (condition) having two levels (low and high response predictability sentences or stems with low and high selection demands), and the third factor (task) having three levels (SCP, SCW, STC). The order of presentation of tasks, their subdivision in blocks, so as the division of high-low stimuli within each block were varied exactly as in experiment 1; the only exception was that, in experiment 2, half subjects (12) were administered the first series of three blocks while carrying out the LD version of the motor task, and the second series of three blocks while executing the MD version of the task. The reverse order was adopted for the other half of subjects.

Data Analysis

Subjects were generally highly accurate on the motor task. The lowest performance (85%) was obtained in the MD version when, at the same time, subjects had to produce single words to complete high response predictability sentences (SCW task). The highest performance (92%) was instead obtained when subjects were engaged in the LD version while simultaneously completing stems with low selection demands. Given the high accuracy of subjects on the motor task, these data were not analysed further. The analyses on RT performance of the different language tasks were carried out either including only verbal responses given while subjects were 100% accurate on the motor task, or all verbal responses regardless of the performance on the distracting motor task. No significant differences were obtained for RT between these two conditions. Thus the analyses which follow are based on all verbal responses (i.e. RT obtained without filtering for accuracy in the motor task).

Moreover, only 3.6% of the trials were excluded from the analysis as trials in which subjects did not give any verbal response.

Results

RT performance on each of the three tasks is reported in figures 2.3 (sentence completion by mean of phrase generation, SCP), 2.4 (sentence completion by mean of single word generation, SCW), and 2.5 (stem completion, STC). A 2x2x3 repeated measure ANOVA was carried out involving the factors of dual-task (less demanding: LD, more demanding: MD), Condition (high and low), and Task (SCW; SCP; STC). The analysis revealed main effects of Condition (F (1, 23) = 11.62, p < .01), and Task (F (2, 46) = 24.64, p < .001), a Dual-task x Condition interaction (F (1, 23) = 8.93, p < .01), a Condition x Task interaction (F (2, 46) = 4.39, p < .02), and the three-factors Dual-task x Condition x Task interaction (F (2, 46) = 4.45, p < .02). Post hoc tests (using Bonferroni corrections) indicated that SCP was the slowest task (p < .001 for both contrasts SCP vs. SCW and SCP vs. STC), and that SCW was faster than STC (p < .017). Moreover, in view of three-factor interaction, we analysed the critical Dual-task x Condition interaction within each task separately. A 2 x 2 repeated measure ANOVA was performed, for the SCP task, involving the factors of Condition (high and low) and Dual-task (LD, MD). The Dual-Task x Condition interaction was obtained from this analysis (F (1, 23) = 8.30, p < .01), but the main effects were not significant. Post hoc tests indicated that the interaction was due to low response predictability sentence completion that was slower in the MD version of Dual-Task than in the LD condition (p < .04). No such difference was found for high response predictability sentence completion (p = .27). Moreover, low response predictability sentences were slower to be completed than high response predictability ones in the MD version of the motor task (p < .03) but not in the LD condition (p = .11) (see figure 2.3).

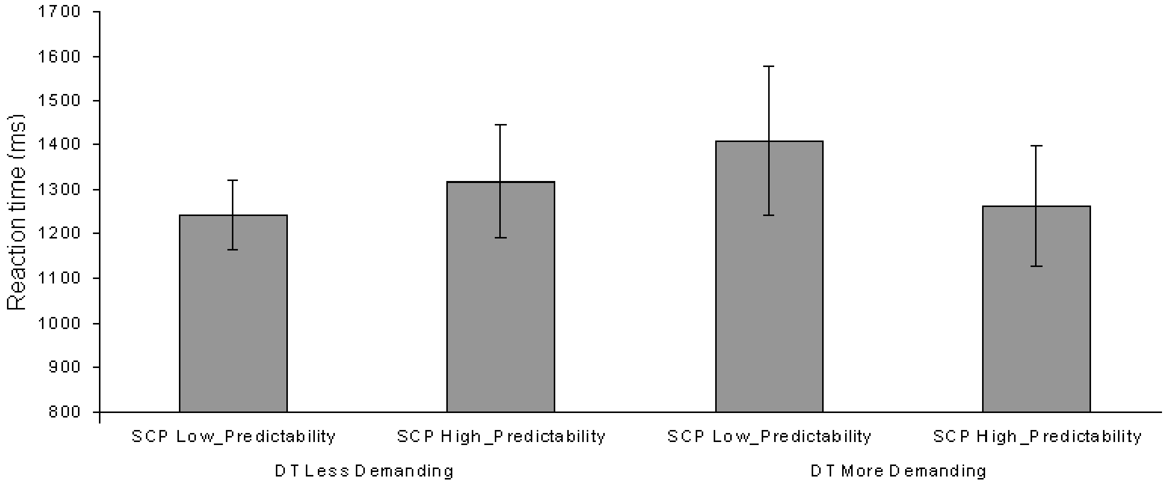

Figure 2.3: Mean reaction times as a function of task (x-axis). Sentence completion by mean of phrase generation (SCP) is presented in its two conditions (i.e. low-high response predictability) for each condition of the dual task (DT). Vertical lines depict standard deviations of the means.

A similar 2 x 2 ANOVA was carried out for the SCW task; this analysis showed a significant main effect of Condition (F (1, 23) = 11.17, p < .01), as well as the two-factor Dual-task x Condition interaction (F (1, 23) = 6.03, p < .03). The main effect of Dual-task was not obtained. In a similar way to the SCP task, post hoc tests were employed for the SCW task and indicated that the interaction was driven by low response predictability sentence completion that was slower in the MD version of Dual-task than in the LD condition (p < .02). No such difference was found for high response predictability sentence completion (p = .37). Moreover, low response predictability sentences were slower to be completed than high response predictability ones in the MD version of the motor task (p < .01) but not in the LD condition (p = .23) (see figure 2.4).

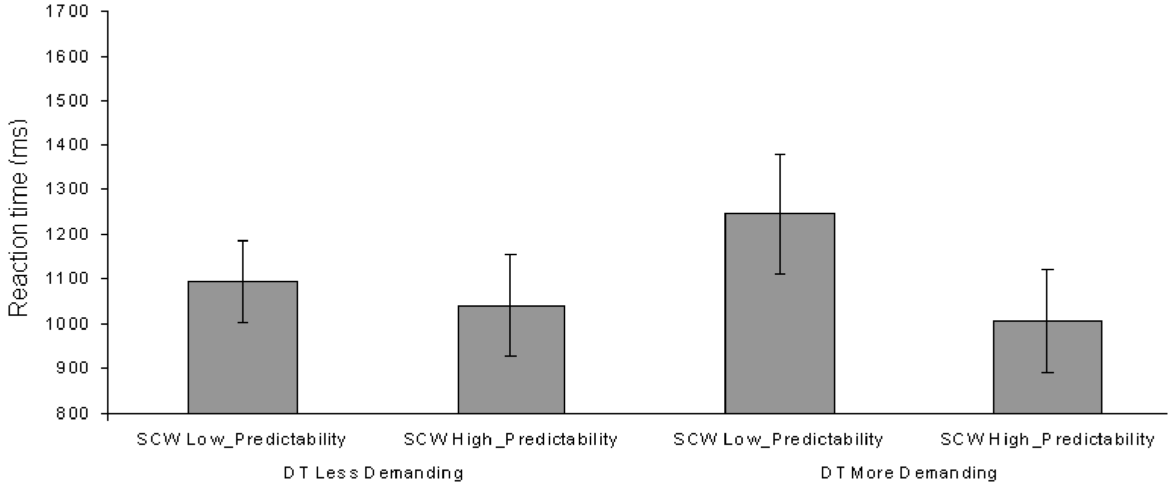

Figure 2.4: Mean reaction times as a function of task (x-axis). Sentence completion by mean of word generation (SCW) is presented in its two conditions (i.e. low-high response predictability) for each condition of the dual task (DT). Vertical lines depict standard deviations of the means.

Finally, a 2 x 2 ANOVA involving the factors of Condition (high and low) and Dual-task (LD, MD) was also carried out for the STC task. Such an analysis failed to show any significant main effect or interaction (see figure 2.5).

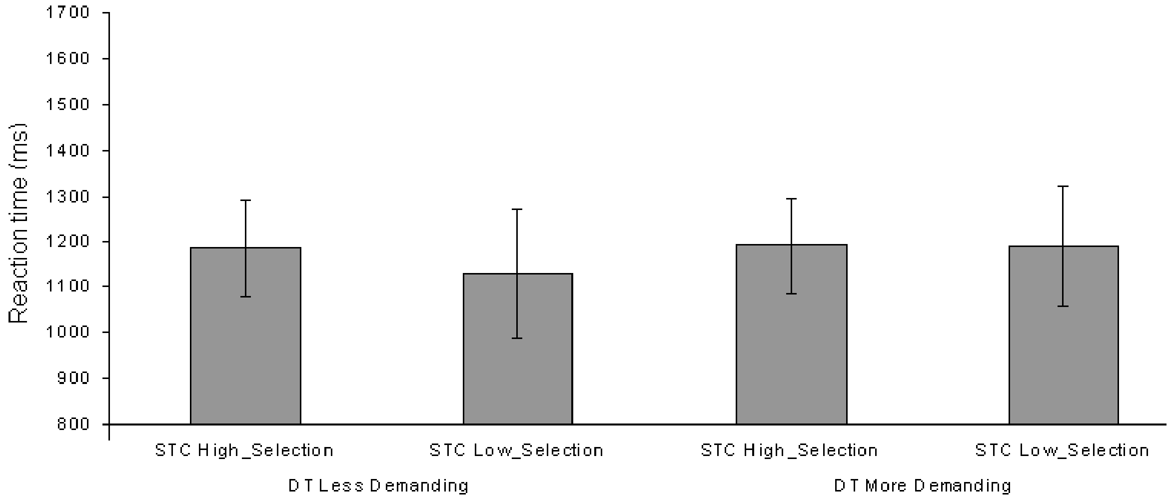

Figure 2.5: Mean reaction times as a function of task (x-axis). Stems completion (STC) is presented in its two conditions (i.e. low-high selection demands) for each condition of the dual task (DT). Vertical lines depict standard deviations of the means.

Summary of experiments 1 and 2

Results of experiments 1 and 2 clearly support the predictions. Findings from the first experiment show that low response predictability sentences take longer in order to be completed than high response predictability ones. Globally, more time is required in order to complete a sentence by mean of an entire phrase than through a single word. Finally, irrespective of differences in selection demands, different stems are completed in the same amount of time once that the completions are matched for frequency. Results from the second experiment showed that the more demanding version of a concurrent motor task specifically influences performance on the low response predictability sentences but not on stems with high selection demands.

2.9. General Discussion

Both the single case analysis and the behavioural experiments have shown that selection of responses from among competing options is generally associated to worse performance than selection of responses that are more uniquely related to stimuli. Nevertheless, this was not always the case in normal adults since analogue performance was obtained, in the stem completion task, for stems which differed in selection demands (i.e. high and low). Results obtained from the behavioural studies have also shown that the effects are mainly restricted to RT (i.e. increased RT for low response predictability sentences) in normal adult subjects. On the other hand, OTM's performance on the sentence completion tasks clearly indicated that, following a lesion involving fronto-striatal circuits, the ability to select task-relevant responses in situation of high competition may be gravely compromised.

As already shown, several investigations of dynamic aphasic patients have accounted for the observed verbal output deficits in terms of inability to select a response from among alternative options (Robinson et al., 1998; Robinson et al., 2005). The lesions of the patients reported in these studies also suggest the importance of the left inferior frontal gyrus for the selection of task-relevant responses and this is clearly in line with the considerable amount of evidence, briefly reviewed in the Introduction, which emphasizes the role of this brain region in conflict resolution (Thompson-Schill et al., 1997; 1998; Barch et al., 2000; Persson et al., 2004; Zhang et al., 2004; Moss et al., 2005). Accordingly, we have previously discussed the possibility that OTM's difficulty in generating verbal responses in situation of high competition may relate to a frontostriatal damage disrupting the left frontal region function of selection in situation of high competition. The results of the behavioral experiments, in particular of the second of these, are in line with such a proposal. In the second behavioral experiment, adult subjects were asked to complete sentences, either with phrases or single words, and stems while at the same time executing a motor task. Critically, RT increased when subjects had to produce single words or phrases in order to complete low response predictability sentences while simultaneously performing the more demanding version of the motor task. As already shown, this kind of distracting task has been described to affect performance of some tasks which require PFC (Moscovitch, 1994; Fletcher et al., 1998). Thus, a possibility is that low response predictability sentences rely more on the operations of the left PFC than high response predictability sentences because the former require more processing demands than the latter; this would be due to the need of selecting a response from among others in competition in the case of sentences with low predictable responses.

The finding of the analogous RT for the *many* and the *few* stems as well as the fact that the more demanding version of the dual-task does not influence the performance on the *many* stems, suggest that both conditions of the stem completion task require similar processing demands despite the differences in selection demands. As already shown, it is possible that stem completion mainly reflects the frequency values of the completion words rather than selection between different words. Thus in both high and low selection demands conditions the same attentional resources may be necessary to select the completion with the highest frequency. In other words, bottom-up activation of the target representations (i.e. high frequency completions) may be sufficient to result in recovery of the relevant information in both conditions of the stem completion task that we used. Selection of task-relevant responses may occur in a more automatic way in the stem completion task than in the low response predictability sentence completion conditions. As stated by Badre and Wagner (2002) strong associative strength between stimulus and response (that may be given by high frequency words that act as completion in the stem completion task) can drive automatic retrieval, irrespective of the number of word competitors and without any behavioural cost (i.e. similar RT for high and low selection demands stimuli).

In the second part of the thesis (Chapters 4, 5 and 6) we investigate further how stimulus-response association strength and selection demands influence retrieval of task-relevant responses. This will be done using both verb and noun generation tasks which were administered to populations of young adults, older controls, and PD patients. Such investigations are also important to better understand *how* PFC and BG contribute to the selection of task-relevant responses.

Chapter 3

3.1. Aim of the COGENT computational model

In the second chapter we investigated the ability to select responses from amongst alternative options both on a dynamic aphasic patient (OTM) and normal adult subjects. As far as the sentence completion task is concerned the data have shown that sentences with low predictability of the response (i.e. with many response options) are harder to complete than those with high predictability of the response (i.e. with few response options). More specifically, results obtained on normal adults show that low response predictability sentences are slower to be completed than the other kind of sentences; on the other hand, findings on OTM have shown that low response predictability sentences are completed much less often than the high response predictability ones. Thus, the case of OTM suggests that the ability to select a response when others compete may be dramatically disrupted after lesions involving fronto-striatal circuits. As reported in Chapter two, an impairment in creating preverbal messages (Levelt, 1989; 1999) has been proposed to account for dynamic aphasics' difficulties in selecting verbal responses from amongst alternatives. For instance, Robinson et al. (2005) claimed that this kind of patients have defective mechanisms of conceptual preparation of language. At this level, lexical concepts have to be generated, sometimes in conditions of high competition, namely when many of them are simultaneously activated.

In this chapter we describe a computational model, implemented in the GOGENT information processing package (Cooper, 2002), which aims to address some of the processes of conceptual preparation of language production. Generally speaking, models of speech production (see Levelt, Roelofs, & Meyer, 1999, for a review) assume an initial stage of conceptual preparation, a successive phase of lexical encoding and a later stage of phonological output organization. In most of these models the processing stages involved in lexical and phonological encoding are much better explained than those occurring at the level of conceptual preparation. In particular, Roelofs (1992; 1997) has proposed a detailed computational framework, the so called WEAVER model, which covers the stages from lexical encoding to syllabary access.

A second important aim of our COGENT model was to shed light on the language output deficit of patients with dynamic aphasia. To this purpose the model focuses on a sentence completion task of the kind of that administered to OTM (and also to normal adults). A series of simulations were also run in order to reproduce and explain the patterns of intact and impaired performance that normal subjects and OTM respectively showed on the task. Although our model was a simplified one, it has provided interesting evidence on the mechanisms of conceptual preparation of language and on the kind of deficit involved in dynamic aphasia. Our simulations have shown that OTM's problems in verbal response selection in situations of high competition could occur because of an abnormal balance between the values of a self activation parameter and a lateral inhibition parameter of an interactive activation network. As reported in the Introduction, this fits with the suggestion that fronto-striatal circuits may operate to filter task-irrelevant information in order to allow selection of task-relevant responses.

Before introducing the model, it is helpful to give a brief description of both the processes which operate at the conceptual level of the language production system and the principles of first-order logic which was used to support inferences about communication.

3.2. Conceptual preparation of language

In his pivotal book, Levelt (1989) has proposed a detailed architecture for the processing system that underlies speech production. The architecture consists of various processing components that allow speakers to translate intentions into overt speech. Each component is conceived to produce its own characteristic output representations. These are, respectively, lexical concepts, lemmas, morphemes, phonological words, and phonetic gestural score (Levelt et al., 1999; see figure 3.1). Dynamic aphasia is thought to involve the highest component of the architecture, namely the process leading up to the activation of lexical concepts, which is known as conceptual preparation.

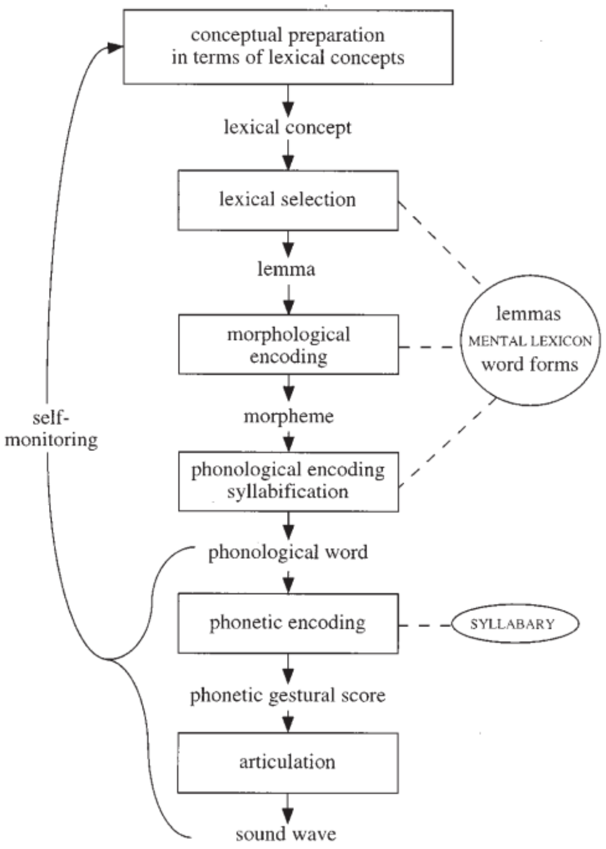

Figure 3.1. Levelt, Roelofs, & Meyer's (1999) theory. Word production involves the stages of conceptual preparation, lexical selection, morphological, phonological, and phonetic encoding, and articulation (Levelt, Roelofs, & Meyer, 1999).

As claimed by Levelt (1989), speaking involves thinking about an intention, selecting the relevant information that has to be expressed for the realization of this intention, ordering the information for expression, and keeping track of the current discourse. The sum of all these processes consists of the conceptual preparation of language whose product is a *preverbal message*. In more detail, planning an utterance comprises an early stage in which the speaker decides on the purpose of his/her next communicative act. The speaker has to select the information whose expression realize his/her communicative goals. In the situations in which the information to be expressed is complex, because of many successive communicative goals that need to be satisfied, the speaker will have to decide how to order the information for expression. Moreover, the speaker also needs to take into account the state of the discourse so far in order to choose that particular concept whose expression will achieve that particular communicative goal; in other words an utterance needs to be specified from an informational perspective. On Levelt's theory, the generation of communicative intentions and the selection of information for expression take place in the *macroplanning* stage in the planning of preverbal messages, whereas perspective taking is carried out by the *microplanning* stage.

During sentence encoding, the early pre-verbal message consists of a semantic structure in which several lexical concepts are retrieved and linked together. Lexical concepts are also activated during single word production; they are involved in the process of lexical-semantic retrieval through which verbal expression can be accessed later (Levelt et al., 1999). Thus lexical concepts are concepts for which there exist words in the speaker's language. A critical aspect of Levelt et al.'s theory (1989; Levelt et al., 1999) is that lexical concepts are not represented by sets of semantic features but as individual wholes. Thus in a conceptual network there may be an independent (preverbal) message element which is related to the concept node of, for instance, *GUIDE (X, Y)* that in turn stands for the meaning of the lemma *"to guide"*. Moreover, following Levelt et al.'s theory (1999), nodes in the conceptual network are linked to other semantically related nodes. During the process of intention formulation, activation spreads over a conceptual network, so that many candidate concepts may be active at once. This results in the parallel activation of the corresponding lemmas which compete with each other for selection. Because of this mechanism, selection of a new word may occur with different probabilities and at different latencies depending on the degree of simultaneous activation of other lemmas.

Our model focuses on the macroplanning processes since the findings on our dynamic aphasic patient (see chapter 2) suggest that the main problem in the syndrome lay in the selection of the relevant information for expression (macroplanning) rather than in determining the informational perspective of an utterance. The model defines the processes involved in encoding and selecting messages which act as candidate sentence completions.

3.2.1. Macroplanning

Generally speaking we produce utterances in order to realize some communicative intentions such as informing another person about something. As proposed by Levelt (1989), an utterance with communicative intention has *illocutionary force* and is called a *speech act.* Thus, a speech act is an intentional action performed by mean of an utterance (Levelt, 1989, p. 58). Macroplanning involves the elaboration of some communicative goals into a series of subgoals and its output represents a sequence of speech act intentions, that is, messages identified for both mood (e.g. declarative, interrogative, imperative) and content.

According to Levelt (1989), in order to encode a message, a speaker has to have access to two kinds of knowledge: declarative and procedural. The latter takes the form of a series of condition-action pairs whereby IF certain conditions are verified THEN a certain action can be performed (see Introduction). For instance, IF the intention is to commit oneself to the truth of *p*, THEN assert *p*. Thus the conceptual preparation of language can be conceived as a structured system of such condition-action pairs. As shown in the Introduction, these procedures can deposit their results in working memory which, in turn, maintains the information attended to by the speaker. The other kind of knowledge is declarative knowledge, a major kind of this being the propositional knowledge. A unit of propositional knowledge may be given, for instance, by the value: *p* = *"In summer it is hot"*. Propositional knowledge like this is generally available in long-term memory.

As shown above, each speech act begins with the conception of some communicative intentions. For each speech act to be effective the addressee must be able to recognize the speaker's intention to communicate some information *p*. Thus the speaker's communicative intention must also involve the intention that the utterance makes it possible for the addressee to understand the speaker's goal to convey a certain thought. In other words, a communicative intention always involves the purpose of intention recognition by the addressee. An *informative* speech act is a simple example that helps understanding how macroplanning serves the passage from intention to message. A speaker (S) may want to tell the hearer (H) that a third person (TP) is a good scientist (GS). S' message encoding may begin with the goal (intention) to let H know that S intended H to believe that TP is a GS. More formally, such a communicative intention is given by the following expression:

1) KNOW (H, INTEND (S, BELIEVE (H, GS (TP))))

The speaker may realize his communicative intention by encoding a declarative sentence whose message would be expressed by: *2) DECL (GS (TP))* (uttered as: *The third person is a good scientist).* At the macroplanning level, a general message encoding procedure for this informative speech act would be given by the following rule:

IF the goal state is *KNOW (H, INTEND (S, BELIEVE (H, GS (TP))))*
THEN encode message *DECL (P)*

Generally, going from the first kind of expression (intention) to the second (message) requires more than a single step. The conditions of rules similar to the one above need to be specified and this can reflect in the addition of other rules and subgoals. To give an example, the speaker must initially believe that the hearer does not know yet the proposition *p* and this requires that some subgoals are fixed.

3.3. A First-order theory of communication

Our model is based on First-order logic in order to support inferences about planning, knowledge and, most important for our aims, communication. The theory supports communications and plans for both informative statements and requests which are the speech acts of interest in our model. In our proposal the speaker is the agent of the model and can either complete a sentence or request the hearer to do this when the agent does not know how to complete the sentence (i.e. no knowledge about the sentence is stored in the speaker's general knowledge). In order to reason about knowledge we first provided the model with a suitable series of axioms (Hintikka, 1962) (see below) to express facts about the grossly simplified agents' world considered in the model, that of sentence completion. All the axioms we used were expressed with operators for knowledge and intention. According to Appelt (1985) utterance planning requires reasoning about different types of intensional operators. Our model refers to four kinds: *Intend* (intending to construct a true proposition), *Intend-to-do* (intending to perform a communicative action), *Know-ref* (knowing the denotation or referent of a description) and *Know*. To give an example of knowledge that the hearer and the speaker share in the model, we can consider the following:

know(S, intend(H, intend_to_do(P, Complete)))

This statement declares that the speaker (S) knows that the hearer (H) intends to make the request (to the speaker) to complete the sentence (P). The axiom system reported in the model is the following (P and Q refer to knowledge facts and S to the agent):

A1. (true(P), true(P))
A2. ((know(S, P), know(S, implies(P, Q))), know(S, Q))
A3. (know(S, P)), true(P)
A4. (know(S, P)), know(know(S, P))
R1. ([implies(P, Q), true(P)], [true(Q)])
R2. ([true(P)], [true(know(P))])

A1 expresses all instances of propositional tautologies, and together with the modus ponens (R1) they are taken from propositional logic. A2 says that an agent's knowledge is closed under implication; A3 says that an agent only knows things that are true. This axiom usually distinguishes *knowledge* from *belief.* A4 is an axiom of introspection and says that an agent is introspective, that is he can look at his knowledge base and knows what he knows. Finally R2 is the rule of necessitation.

Recently Davis & Morgenstern (2005; see also Appelt, 1985) have proposed a theory, expressed in first-oder logic, for supporting inferences about planning and communication. In more detail, their theory supports both the representation and communication of information and requests and involves physical states, knowledge states, and informative communications. Following these authors, the *informative* and *request* speech acts are described at three different levels of abstraction at the different stages of our model.

- At the physical level, *communicate(C)* where C can be instantiated as inform or request. A communicate event occurs whenever an utterance action occurs. The representation at this level expresses the event of the speaker that commits himself to communicate something to the hearer. The primitive communicate does not specify the content of the communication.
- At the illocutionary level in which we have: a) *request(S, H, P)* expresses that the speaker, S, is to make a request to the hearer, H, of executing plan P that is about completing the sentence; and b) *inform(S, H, P)* expresses that the action of the speaker, S, will be to inform the hearer, H, about the plan, P, of completing the sentence.
- At the locutionary level, a) *do(S, request(S, H, Q))* requests that the atomic action of the speaker, S, is of requiring the hearer, H, to complete the sentence using the proposition Q; b) *do(S, inform(S, H, Q))* expresses that the atomic action of the speaker, S, is to inform the hearer, H, about the proposition Q. Proposition Q is always concerned with a candidate completion of the initial sentence that the hearer required the speaker to complete.

Important features of speech acts are their epistemic effects. The case of a speaker informing a hearer about a proposition *Q* will have effects on the agents' knowledge states. When communication is finished, both the hearer and the speaker know that the communication has taken place; furthermore both the hearer and the speaker share the knowledge that *Q* was true at the beginning of communication.

3.4. A macroplanning model to simulate dynamic aphasia

3.4.1. Why COGENT?

As reported in the Introduction, COGENT (Cooper & Fox, 1998; Cooper 2002) is an integrated approach to cognitive modelling which supports different styles of modelling (e.g. symbolic models). It provides a set of primitives (e.g. connectionist networks, memory buffers) which are assembled to implement a variety of computational models in different cognitive domains. The boxes of a COGENT model can be configured through the use of properties (e.g. capacity limitations and decay for memory buffers or rate of firing for production rules), the manipulations of which may allow the simulation of specific neuropsychological conditions.

One of the main distinction made in COGENT is between rule-based processes, whose behaviour is expressed in terms of a set of rules, and buffers which are information stores appropriate for both short term storage (e.g. as in modelling working memory) and long term storage (e.g. as in large knowledge bases) (see Cooper, 2002). Processes can read information from buffers and write information into them. A feature of COGENT that makes it particularly suitable for hybrid cognitive modelling is that it allows the use of simple connectionist networks. An example of such a network is given by the *Conceptual Knowledge* component of figure 3.3 (see section 3.4.3) that represents an interactive activation network (IAN). Finally, compound systems with internal structure can also be used in COGENT's models.

COGENT's rule-based modelling language allows complex processes to be specified in terms of production-like rules. Each of these rules consists of a series of conditions and a series of actions. The former include logical operations and/or operations which set variables, such as matching some information stored in a buffer. Actions of a given rule allow information to be sent to other boxes. Rules can also contain user-defined conditions which are generally used to provide increased control over the situations in which rules apply. COGENT also supports the representation of different types of information. The main representational unit of COGENT is the *term;* thus, different types of information require different types of terms. The simplest term in COGENT is that referred to both numbers and atoms. The latter are used to represent symbols that have no internal structures (e.g. *dog*). An important concept for our model is that of *compound term*. This term is built from other terms and is used to represent structured information with arbitrary internal structure. Compound terms allow the representation of the meaning of sentences in terms of representations of the sentence parts. For instance, the meaning of: "*The sun is shining*" can be represented by the compound term: "*shine(sun)*".

3.4.2. The Domino Agent Model

The macroplanning components of our model are embedded in an existent agent framework, the DOMINO framework of Fox and Das (2000) which is a candidate computational implementation of tasks with a planning/executive component. The DOMINO agent model has in fact been proposed as the basis for a SAS model (Glasspool, 2000) since it deals with problems, such as setting of high-level goals, strategy generation, problem solving, and implementation of plans and actions, which are typical SAS problems (Norman & Shallice, 1986). Fox and Das' framework rests on seven types of processes which operate on six types of information (see figure 3.2; types of information are represented by circles and types of processes by arrows).

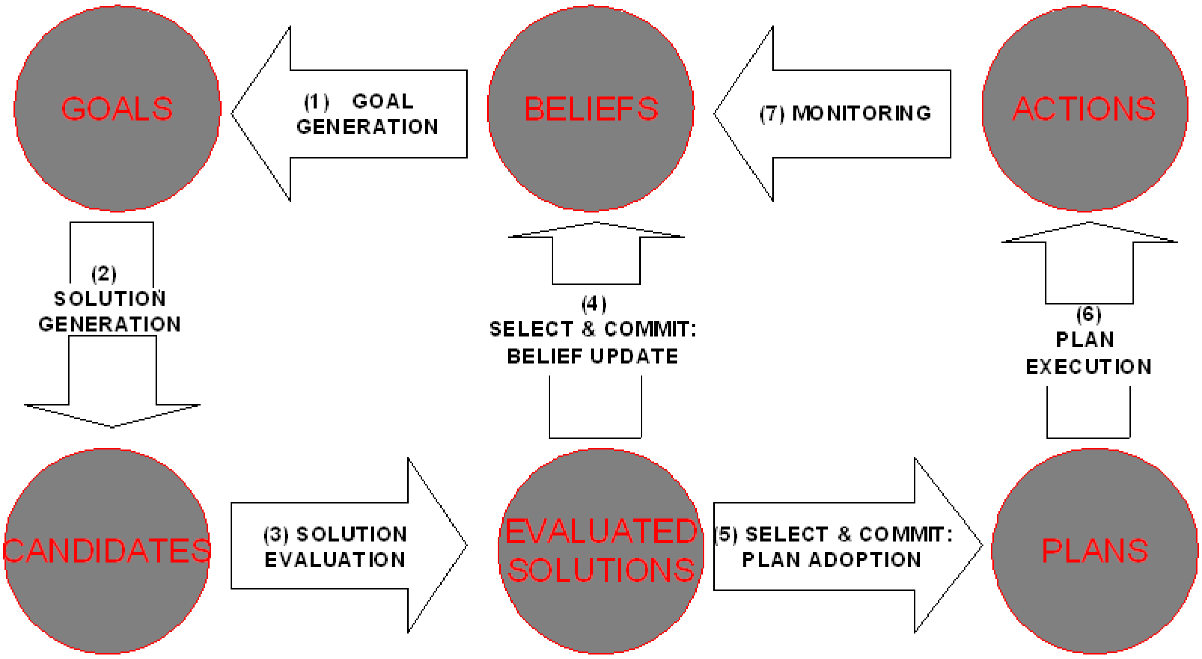

Figure 3.2. The DOMINO agent model of Fox and Das (2000) (picture reproduced from Cooper, 2002).

Briefly, the first process (1) sets one or more *goals* taking into consideration the content of information present in *beliefs*. The second process (2) aims to generate solutions through problem solving procedures. The *candidate* solutions are then evaluated by the third (3) process so that beliefs can be updated (4), or a plan adopted (5) after that a candidate solution has been selected. A given plan is then subdivided into individual actions which are executed by the agent (6). Finally, the last process (7) aims to monitor the effects of the taken actions as, for instance, checking whether these match the initial goal. As shown above, many of the SAS processes may be mapped onto the DOMINO framework (e.g. solution generation, goal setting, planning, solution evaluation, and monitoring), however, as noted by Cooper (2002), the sixth process (*plan execution*) corresponds to the contention scheduling (CS) component of the Norman and Shallice's proposal (1986).

3.4.3. The Macroplanning Model

By basing our macroplanning model of sentence completion on the DOMINO agent framework we can take a step-by-step approach that allows us to gradually increase the complexity of the model and to be confident that the various macroplanning/SAS components operate together in a well-defined way. Following Levelt (1989) we assume that macroplanning requires both declarative and procedural knowledge. Thus, our model consists of a structured system of condition-action pairs expressed as production rules (see appendix 1). These procedures make the processing advancing in the model given that the rules act on a series of buffers changing their contents. Generally, the conditions for production rules concern a series of illocutionary intentions whereas the actions performed are speech acts. As described above, the output of macroplanning is a sequence of speech acts specified for both mood and content. This means that the model has to go through a series of steps in which communicative intentions are defined and contents are recalled. The model hypothesized that the behavior of a subject in the sentence completion task consists of a series of steps. Figure 3.3 shows the overall structure of the model developed within the COGENT environment (Cooper, 2002). In the figure, buffers and processes are indicated in italics and represented respectively by rectangular boxes with rounded corners and hexagons; numbers from 1-12 indicate successive phases of processing in the model.

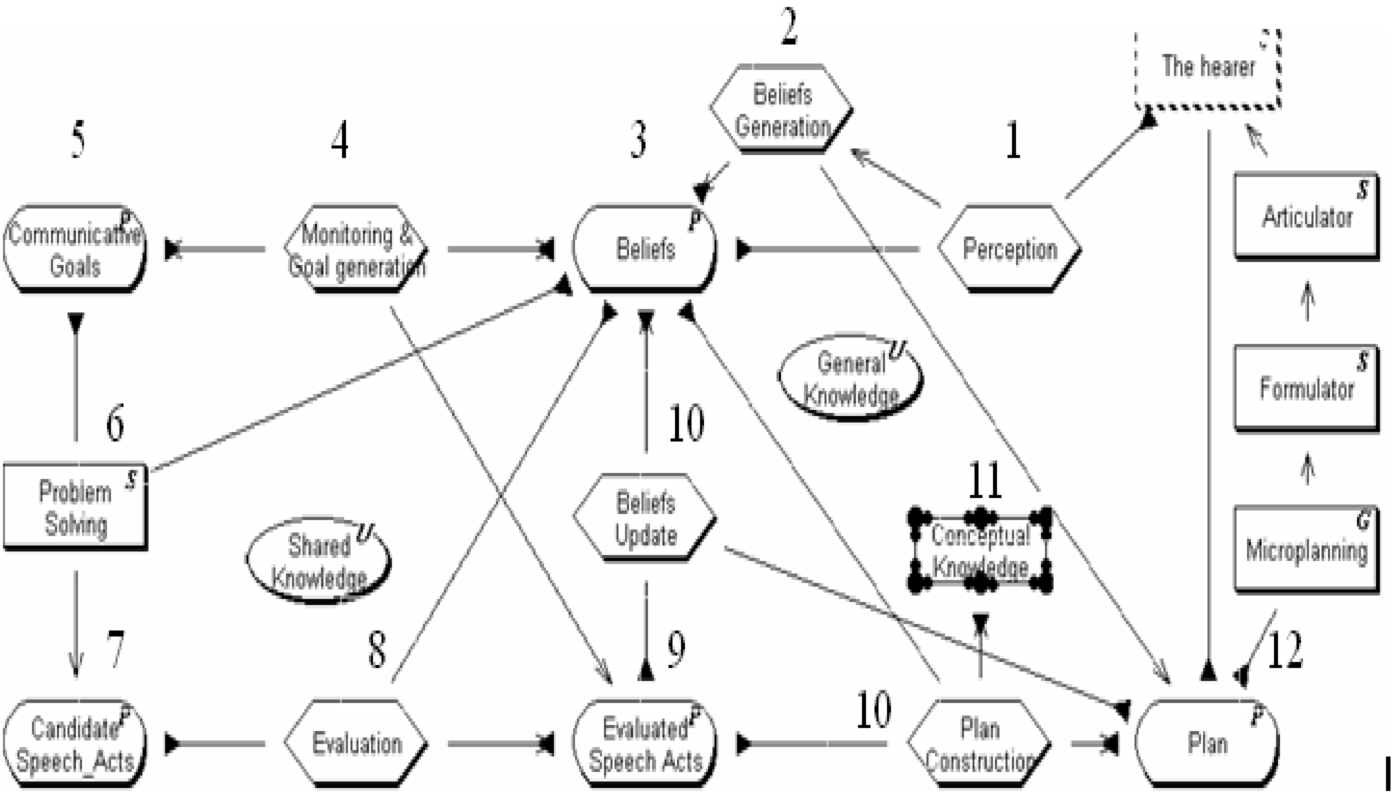

Figure 3.3. Overall structure of the macroplanning model of sentence completion. Numbers from 1-12 indicate successive phases of processing in the model. A series of shallow productions are created within the *Microplanning*, *Formulator*, and *Articulator* compound systems in order to let the *hearer* to give a rudimentary feedback to the speaker. The latter is the agent of the macroplanning model. Rule-based processes are represented by hexagons and buffers by rectangular boxes with rounded corners. Arrows connecting processes to buffers indicate that the former can read information from the latter and write information into them. Moreover, compound systems with internal structure are represented by rectangular boxes (e.g. *problem solving*).

A brief description of the different processing steps of the model is given below. Some of the most representative production rules are also reported in order to explain better the function of some rule-based processes. All production rules are reported in appendix 1.

a) A belief is generated (*Belief Generation*) in order for the speaker to commit himself to accomplish the request (of the hearer) of completing a sentence *(P).* The belief is then sent to the *Beliefs* buffer. The following rule and its condition definition allow the speaker to send the belief of completing a sentence to the *beliefs* buffer.

```
IF:         not request(complete, P) is in Beliefs
            action_of_completion(requeste(complete), [Act])
THEN:       add request(complete, P) to Beliefs
            add [Act] to Beliefs
```

```
Condition Definition: action_of_completion
        action_of_completion(requeste(complete), [intend(S, know(hearer, proposition))]):-
                rule([request(complete)], [_ ]) is in General Knowledge
                know(proposition(Q)) is in General Knowledge
        action_of_completion(requeste(complete), [intend(S, intend_to_do(hearer, proposition))]):-
                rule([request(complete)], [_ ]) is in General Knowledge
```

The rule fires in the situations in which a request of completing a sentence is not already present in *beliefs* and when the *action_of_completion* of a sentence is verified. The condition of *action_of_completion* is defined in two ways. The speaker (S) can either intend to let the hearer knows a proposition (inform the hearer) or he/she can intend that the hearer will produce a completion (intend_to_do operator; this will be the case when the speaker does not know how to complete the sentence). In both cases, *action_of_completion* is verified if the speaker knows (a rule is given in general knowledge) that the hearer's request to complete a sentence gives rise to either an informative or a request action (*Act*). If the conditions of the rule are satisfied, the speaker commits himself (Act) to accomplish the request of completing a sentence (*P*).

b) A communicative goal of the kind "*complete (communicate, generate-sentence)"* is defined through the *Monitoring and Goal Generation* process. Communicative goals are at the physical level of abstraction at this stage (see section 3.3). The rule reported below adds a goal to *communicative goals* if a series of conditions are satisfied (i.e. the request to complete a sentence is in *Beliefs*, no previous speech_act is already in *Beliefs*, both the speaker and the hearer know what the sentence completion task consists of, and the knowledge of how either inform or request is in *Beliefs* (precondition)). The sub-condition definition: "*Axiom is in General Knowledge"* refers to the axioms discussed in section 3.3.

```
IF:             request(complete, P) is in Beliefs
                not current_illocutionaryact(Speech_Act) is in Beliefs
                speaker_knows_task(Generate_sentence)
                rule(C, A) is in Shared Knowledge
                precondition_satisfied(C)
THEN:           add complete(communicate, Generate_sentence) to Communicative Goals

Condition Definition: Test for preconditions of informing

                precondition_satisfied([]).
                precondition_satisfied([H|T]):-
                speaker_knows(H)
                precondition_satisfied(T)
```

Condition Definition: speaker_knows

```
speaker_knows(Inform_known):-
[intend(S, intend_to_do(hearer, proposition))] is in Beliefs
[intend(S, know(hearer, proposition))] is in Beliefs
speaker_knows(Location):-
knowref(Location) is in Shared Knowledge
speaker_knows(Axiom):-
Axiom is in General Knowledge
```

Condition Definition: speaker_knows_task

```
speaker_knows_task(generate_sentence):-
know(S, intend(H, intend_to_do(S, Complete))) is in Shared Knowledge
```

c) *Communicative goals* are expanded into sub-goals (Levelt, 1989). A *Problem Solving* process assures that preconditions for communication are verified. To give an example, a precondition that has to be verified is that the speaker knows that the hearer intends him/her to complete a sentence. A goal stack strategy is adopted for further defining speech act intentions. The problem solving output contains a set of candidate speech acts that have to be evaluated. The representation of the speech acts is at the illocutionary level at this stage and these are stored in the *Candidate Speech_Acts* buffer. As candidates we have: *"do(Speaker, inform (Hearer, P))"* and *"do(Speaker, request(Hearer, P))"*.

d) *Candidate speech acts* are evaluated by the *Evaluation* process. This process comes to a decision of completing the sentence either through an informative or request speech act. The decision depends on whether a fact about the sentence (i.e. a possible way to complete it) is present in the speaker's general knowledge (GK). The speech act with the highest evaluation is selected and stored in the *Evaluated Speech Acts* buffer.

```
IF:       Candidate is in Candidate Speech_Acts
          evaluate(Candidate, Value)
THEN:     delete all evaluation(previous_candidate, previous_act) from Evaluated Speech Acts
          add evaluation(Candidate, Value) to Evaluated Speech Acts


IF:       not selected(Candidate) is in Evaluated Speech Acts
          evaluation(Candidate, Max) is in Evaluated Speech Acts
          not evaluation(Other_candidate, Act) is in Evaluated Speech Acts
          Act is greater than Max
THEN:     add selected(Candidate) to Evaluated Speech Acts
          delete all evaluation(_, _) from Evaluated Speech Acts
```

Condition Definition: Evaluate Candidate illocutionary_acts

```
evaluate(do(S, inform(H, P)), 1):-
[intend(S, know(H, proposition))] is in Beliefs
evaluate_through_GK(true)
discourse_focus(Focus)
evaluate(do(S, request(H, P)), 1):-
[intend(S, intend_to_do(H, proposition))] is in Beliefs
evaluate_through_GK(false)
discourse_focus(Focus)
evaluate(do(S, request(H, P)), 0):-
[intend(S, intend_to_do(H, proposition))] is in Beliefs
evaluate_through_GK(true)
discourse_focus(Focus)
evaluate(do(S, inform(H, P)), -1):-
[intend(S, know(H, proposition))] is in Beliefs
evaluate_through_GK(false)
discourse_focus(Focus)
```

Condition Definition: discourse_focus

```
discourse_focus(Focus):-
request(complete, P) is in Shared Knowledge
```

Condition Definition: evaluate_through_GK

```
evaluate_through_GK(true):-
fact(past(Q)) is in General Knowledge
about(Q, children)
evaluate_through_GK(false):-
not fact(past(Q)) is in General Knowledge
about(Q, children)
```

Condition Definition: about

```
about(Proposition, Topic):-
Proposition is composed of List
Topic is a member of List
```

The first rule looks for candidate speech acts in the relative buffer and adds the evaluated candidates to the *Evaluated Speech Acts* buffer. The second rule checks which speech act has the highest evaluation in the *Evaluated Speech Acts* buffer and, as an action, the rule selects this candidate. The first condition definition is about speech acts evaluation. Our model considers only informative and request speech acts. They can be assigned different values depending on whether the condition *evaluate_through_GK* is true or false. This condition is true if a *fact (Q)* about the sentence that has to be completed is in the speaker's GK, while it is false if no fact is present in GK. The sub-condition *about(Q, children)* refers to facts about children since, in this example, the sentence that the hearer asked the speaker to complete was: “*The children were..*”.

e) In the situations in which the selected speech act is one of request, a *Plan construction* process creates a plan that the speaker will use in order to make the request to the hearer to complete the sentence (*P*). The first rule below is aimed to deliver a plan of request to the *plan* buffer. However, when the selected speech act is one of informing, an interactive activation network is activated by *Plan Construction*. The network (*Conceptual Knowledge* in the model) consists of all the facts in the speaker's GK about the sentence (*P*) that has to be completed. The second rule below also checks whether an informative plan is not already present in *plan*. If the conditions of the rule are verified it adds the facts *Q* to the *conceptual knowledge* connectionist network.

```
IF:        [H] is the list of all Speech_Act such that Candidate is in Evaluated Speech Acts
           not plan(do(S, request(H, P))) is in Plan
           knowref(speaker(S)) is in Shared Knowledge
           knowref(hearer(H)) is in Shared Knowledge
           selected(do(S, request(H, P))) is in Evaluated Speech Acts
           propositional_completition(false, P, Q)
           get_information_onP(Unknown, Question)
           [intend(S, intend_to_do(hearer, proposition))] is in Beliefs
THEN:      delete all plan(X) from Plan
           add plan(Question) to Plan

IF:        [H] is the list of all Speech_Act such that Candidate is in Evaluated Speech Acts
           not plan(do(S, inform(H, P))) is in Plan
           knowref(speaker(S)) is in Shared Knowledge
           knowref(hearer(H)) is in Shared Knowledge
           selected(do(S, inform(H, P))) is in Evaluated Speech Acts
           propositional_completition(true, P, Q)
THEN:      add Q to Conceptual Knowledge
           send excite(Q, 0.200) to Conceptual Knowledge
```

Condition Definition: get_information_onP

```
           get_information_onP(not_know_P, do(S, question(past(H, 'the children were')))):-
           rule([_], [do(S, question(H, P))]) is in General Knowledge
```

Condition Definition: propositional_completition

```
           propositional_completition(true, 'the children were', decl(past(Q))):-
           fact(past(Q)) is in General Knowledge
           about(Q, children)
           propositional_completition(false, 'the children were', decl(past(Q))):-
           not fact(past(Q)) is in General Knowledge
           about(Q, children)
```

f) In similar fashion to how competition between schemas operates within the Norman and Shallice's CS system (see next section), in our model each speech act intention has an associated activation level and influences other speech acts in an IAN (*conceptual knowledge* box of figure 3.3). A selection process operates on this network and the selected speech act will be the input to the microplanning system. The network consists of all the facts about P expressed at the locutionary level. For instance, if the initial sentence is *"The chidren were..."* one of its possible completion is expressed as: "*decl(past(go(children(school))))"* at this level. This fact defines an informative speech act intention specified for mood *(declarative)* and content *(children(school)).* The activation of each speech act intention is initially fixed at 0.2 by *Plan construction* (see the second rule above). A speech act intention is selected if it is the most active and its activation exceeds the threshold of 0.8. As shown in the Cooper's (2002) model of the WCST test, such a threshold value suffices to reliably select schemas (i.e. card-sorting schemas representing alternative strategies in his model) which are activated by SAS input (i.e. *plan construction* in our model). The number of processing cycles spent on stage 11 of the model (i.e. on the IAN) depends on the time required by a speech act intention to overcome the threshold. It can also be the case that no speech act reaches the value of 0.8; this has the effects that the processing stops and no plan is delivered to the *plan* buffer.

g) When a speech act intention "wins" the competition in the IAN, *Plan Construction* constructs a definitive plan and sends it to *Plan.* The final plan consists of a speech act intention expressed at locutionary level such as:

do(Speaker(inform(Hearer, decl(past(watch(children, television))))))

This speech act intention constitutes the product of Macroplanning; a preverbal message will be completed by microplanning processes (not modelled). Moreover, the formulator and the articulator processors (not modelled) will allow the speaker to actually complete the initial sentence.

h) A series of shallow productions (see below for one example of this kind of production rule; see appendix 1 for all productions) were created within the compound systems of *Microplanning, Formulator,* and *Articulator* to let the hearer gives rudimentary feedbacks to the speaker. The feedbacks concern the speaker's attempts to complete the sentences. In the model the agents may either share or not the knowledge about a specific completion. If a potential way of completing the sentence *P* is present in the *shared knowledge* system of the model, the feedback will be positive and the processing halts (see rule below); otherwise the feedback will be negative and the speaker will have to choose another completion for the initial sentence. We used the feedback property to investigate how beliefs and plans are revised.

```
IF:             phrase_completed(X, P) is in Prepare feed-back for subjects
                not feedback(F) is in Prepare feed-back for subjects
                plan(do(S, inform(H, decl(Q)))) is in Subject:Plan
                fact(Q) is in Subject:Shared Knowledge
THEN:           send feedback(correct) to Talk to the subject
                add feedback(correct) to Prepare feed-back for subjects
                add feedback(correct) to Subject:Shared Knowledge
                delete phrase_completed(X, P) from Prepare feed-back for subjects
                send stop to Macroplanning
```

The macroplanning model was tested on the sentence completion task and a simulation was run in order to reproduce the performance of both young adults and patient OTM on this task. The next section describes the simulation.

3.5. Cognitive simulation

3.5.1. Rationale and procedure of the simulation

We provided the model with three kinds of sentences; there were 5 low response predictability sentences of the kind used with patient OTM (e.g. *The children were...*) and 5 high response predictability sentences (e.g. *The children went to the park and…*). Another kind of sentence was also included in the model; these were sentences for which we assume the speaker did not have any relevant knowledge. The selection of a speech act of request should allow the speaker to ask the hearer to complete the sentences in these situations. This third type of sentence is not discussed further since the focus of our simulation was on the high and low response predictability sentences. We provided the *general knowledge* (GK) system of the macroplanning model with five facts for each sentence with low predictability of the response (see appendix 1 for the facts that concern the sentence: *the children were…*). On the other hand, only two facts were added to the GK system for each sentence with a high predictability of the response. A simulation of the sentence completion task was finally developed in order to evaluate the model.

As already shown, in the case of an informative speech act an IAN is activated by *plan construction*. IANs contain nodes with associated activation values. In our model all the facts related to a given current sentence are activated in the network. The connections between the nodes of an IAN are, in general, bidirectional making the network interactive (i.e. the activation of one unit both influences and is influenced by the units to which it is connected). IANs exhibit a number of interesting dynamics including: a) *Decay*: the tendency for a unit to return to the rest value; b) *Boundaries*: the tendency for a unit to remain between the max and min values; c) *Equilibrium*: the point to which a network will settle; d) *Competition*: the tendency for units connected by negative weights to turn each other off. A unit that begins with a small advantage eventually "wins" the competition and becomes active at the expense of the other units in the network; e) *Resonance*: the tendency for units connected by positive weights to make each other active and keep each other active in the face of external competition. Moreover, the information processing within an IAN requires time. As shown above, time is measured in “cycles” and during each of these all nodes compute their activation levels in parallel.

In COGENT, boxes consisting of IANs contain nodes with associated activation values. Nodes within an IAN may be created or deleted, and they can be excited or inhibited. In a COGENT model, an IAN co-exists with a process (e.g. *Plan construction*) which sends excite or inhibit messages to control the node activations. On each processing cycle, the total excitation/inhibition to each node within the network is summed. This net excitation/inhibition is then used, along with the node’s current activation and network activation properties to determine the new activation of each node. In addition to external input, node activations may be subject to internal competition, using properties such as Lateral Inhibition and Self Activation. The network’s behaviour can also be regulated using other general properties as well as properties which deal with network initialisation. The node whose activation exceeds a given threshold is generally selected in an IAN.

In the macroplanning model we used an IAN characterized by the parameters reported in table 3.1. We mainly employed the values used by Cooper and Shallice in their implementation of CS (2000) and by Cooper (2002). The self parameter and the lateral parameter are reported in bold being the parameters which were manipulated in the simulation. As will be explained later in the text, Cooper and Shallice acted on these parameters in order to simulate two disorders of intermediate domain action control such as bradykinesia arising from Parkinson’s disease and stereotypy arising from amphetamine psychosis.

Table 3.1

Interactive Activation Network parameters

	Young adults simulation	*Dynamic aphasia simulation*
General properties		
Maximum activation	1.000	1.000
Minimum activation	0.000	0.000
Rest activation	0.100	0.100
Persistence	0.900	0.900
Update function	Cooper and Shallice’s (2000)	Cooper and Shallice’s (2000)
Initialisation		
Initialise	Each Trial	Each Trial
Initial activation	From Normal distribution	From Normal distribution
Act parameter A	0.100	0.100
Act parameter B	0.001	0.001
Self Activation		
Self parameter	**0.770**	**0.745 or 0.770**
Self Baseline	Minimum activation	Minimum activation
Lateral Inhibition		
Lateral influence	Whole net	Whole net
Lateral parameter	**0.205**	**0.205 or 0.23**
Lateral function	Sum	Sum
Lateral baseline	Minimum activation	Minimum activation

Notes: The values of the parameters of the IAN of the macroplanning model are reported for both simulations (i.e. normal adults and dynamic aphasia). The parameters in bold (i.e. self and lateral parameters) are the critical parameters which were manipulated in the simulation. The simulation of dynamic aphasia involves two values for both these two parameters as the data of patient OTM were fitted either reducing the self parameter, relative to the value used in the young subjects simulation, while leaving the lateral parameter unchanged (i.e. 0.745 and 0.205 respectively) or increasing the latter while leaving the former as in the simulation of young subjects (i.e. 0.77 and 0.23 for self and lateral parameters respectively) (see main text for further details).

The general properties of the network concern the maximum and minimum activation that any node may obtain, as well as the value of rest activation to which nodes revert in the absence of excitation and persistence. The latter refers to the degree to which activation values persist in the absence of excitation. Another general parameter is the update function which is used to update the activation of each node on each cycle. In our simulation we used the function that Cooper and Shallice used in their model of CS whose value is bounded by 0 and 1 and tends to *Rest activation* with zero net input (see appendix 1 for the updating activation equation). As far as initialization properties are concerned, we initialized the network at the beginning of each trial (i.e. each sentence); then on initialisation, activations were randomly selected from a normal distribution with mean and standard deviation given, respectively, by the parameters *Act A* and *Act B.* As self activation parameters, *self baseline* was fixed at the minimum activation value. This parameter governs how self activation is calculated. In the present simulation the minimum activation value is subtracted from the node's current activation before multiplying by the *self parameter,* which is a scaling factor, in order to obtain the raw self activation. The self influence of a speech act on its own activation is directly proportional to the speech act activation and such an influence is excitatory in our model. As far as the lateral inhibition parameters are concerned, these were fixed so that all nodes in the network contribute to the inhibition of each node through a *sum* function (i.e. lateral influence fixed at *whole net* and lateral function fixed at *sum* in table 3.1). This means that the inputs from competitor nodes are summed in the network. *Lateral baseline* governs how individual lateral influences from competitor nodes are calculated. Current activations are subtracted from the minimum activation in our network. Similarly to the *self parameter*, the *lateral parameter* is a scaling factor which is multiplied with the output of the lateral function to give the raw lateral inhibition. In more detail, lateral inhibition influences the competition between the nodes of an IAN, and it is generally used to permit that only one node is highly active at any one time (Cooper & Shallice, 2000). In our model, the lateral influence of a speech act intention on another is proportional to the difference between the first speech act activation and minimum activation. As a consequence, the lateral influence of a speech act on competitors is always inhibitory in our network. In general, lateral influence and self influence are opposing sources of activation which, in the absence of any other influence, leave the network in an equilibrium state.

In the attempting to simulate normal adults and patient OTM’s performance on the sentence completion task, we followed the approach that Cooper and Shallice (2000; see also Cooper, 2002) used in their model of CS to simulate the control of routine actions both in normal and pathological conditions (e.g. the action disorganization syndrome). Cooper and Shallice employed a model based on the competitive activation of action schemas and they considered *“the behaviour of the model in parameter space outside of the region that gives rise to normal performance”* (Cooper & Shallice, 2000, p. 323). In the Cooper and Shallice model, the manipulation of one IAN parameter, the so called *Lateral:Self* parameter, was particularly important for the successful simulation of conditions observed in case of BG pathology (e.g. bradykinesia in Parkinson's disease patients). The *Lateral:Self* parameter controlled the proportion of self and lateral influence on the final influence on a node activation in the Cooper and Shallice's model. Accordingly, we varied the lateral inhibition and self activation parameters in our simulation.

We expected that the difficulty in the selection of a response from amongst others in competition, which is often invoked as a potential account for dynamic aphasia (Robinson et al., 1998; 2005), can be reproduced in the model by manipulating the self and lateral parameters. As shown above, the early stages of the macroplanning model are concerned with the setting of communicative intentions and generation of candidate strategies. These operations are likely to be shared by each kind of sentence that has to be completed (either high or low response predictability sentence). Thus, in running the simulation we have assumed that a deficit at these early stages of macroplanning cannot account for the specific deficit of language generation observed in dynamic aphasia.

In sum, for the adult subjects simulation we expect that the model would take longer (i.e. requires more processing cycles) to deliver a plan to *Plan* (point number 12 in figure 3.3) when it is provided with low response predictability sentences than high response predictability sentences. However, accuracy should be similarly high in both sentence completion conditions. On the other hand, the manipulation of the self and/or lateral parameters in the simulation of dynamic aphasia (e.g. increase of lateral parameter or decrease of self parameter) is expected to lead to poor performance specifically on the low response predictability sentences. Thus, in a similar fashion to patient OTM, the model should require even more cycles (relative to the young adults simulation) when given low response predictability sentences, and more importantly, it should fail to complete this kind of sentences approximately fifty % of the times.

For both simulations the model was ran for 100 trials through the10 sentences (10 trials for each sentence). For each simulation, Wilcoxon tests were used to compare the response time (cycles) performance of the model in the two sentence completion conditions. Mann-Whitney tests were instead used to compare corresponding conditions across simulations (i.e. adult subjects simulation vs. dynamic aphasia simulation). Finally, Chi-Square tests were used to compare accuracy performance across the different conditions and simulations.

3.5.2. Results

The best fit for adult subjects data was obtained with values of 0.77 and 0.205 for self and lateral parameter respectively. With these values, the model correctly selected a speech act intention when given both kinds of sentences. As shown in figure 3.4 it only failed in 2/50 trials with the low response predictability sentences (96% accuracy). The difference in accuracy between the two conditions was not significant ($\chi2$ (1) = .510, p = .47). However, low response predictability sentences significantly required more processing cycles than high response predictability ones (Wilcoxon Signed Ranks Test: Z = - 5.205, p < .001, see figure 3.4).

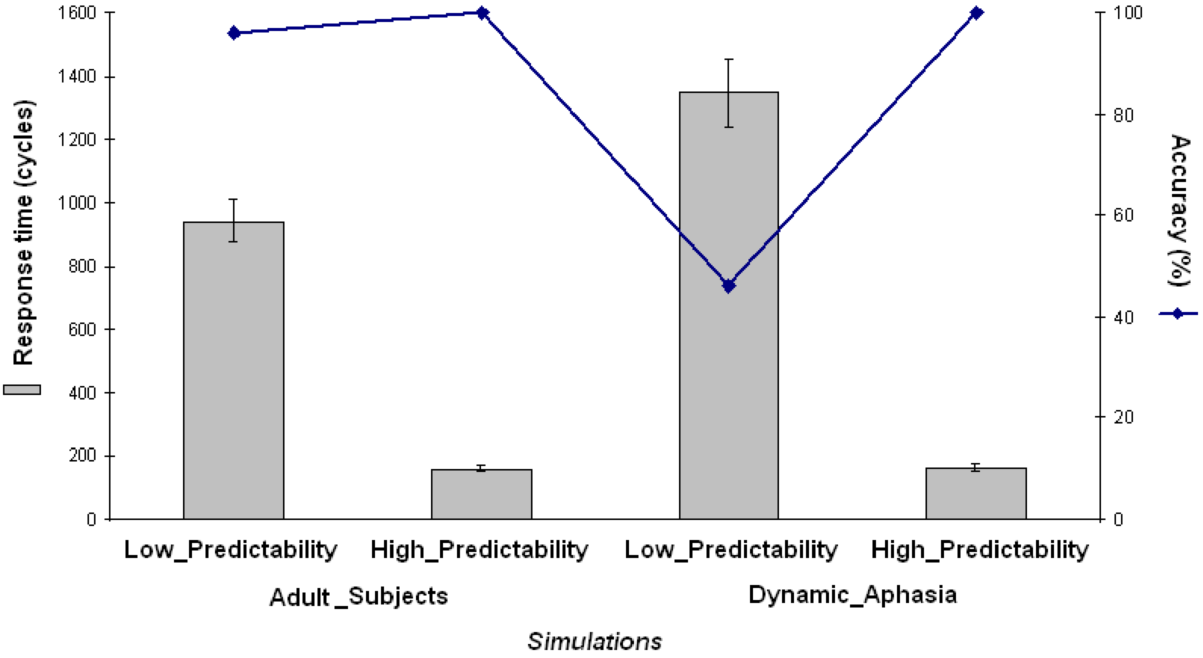

Figure 3.4: Simulation results. The histograms report response time performance, expressed as cycles of processing, for both simulations (adult subjects' performance is showed by the two most left bars and patient OTM's performance is showed by the two most right bars). The blue solid line shows accuracy performance for both simulations. Sentence completion is shown in its two conditions (low and high response predictability sentences). Bars indicate standard errors of the means.

The importance of having an appropriate balance between the values of the self and lateral parameters is suggested by the behaviour of the model when one or both parameters are assigned extreme values (i.e. < 0.1 and > 0.9). Thus, for both sentence types the model was extremely fast in providing *Plan* with a definitive plan when the self parameter was fixed at values of 0.9 or higher, while leaving the lateral parameter at values close to 0.2. The same pattern of results was obtained when the self parameter was fixed to 0.77 but the lateral parameter was changed to 0.1. Moreover, for values of the lateral parameter less than 0.05, disorganization of behaviour appeared. As suggested by Cooper and Shallice (2000), within this region the level of lateral influence is insufficient to ensure successful competition with the effect that, in our model, multiple competing speech act intentions can simultaneously become highly active. Finally, when both parameters were fixed at values close to their maximum or minimum (i.e. both at 0.9 or 0.1) a response was never selected given that all speech acts remained at very similar low levels of activation. In sum, for different values of self and lateral parameters and of their balance, the model expressed different behaviours.

For the simulation of dynamic aphasia we reasoned that for particular values of the two parameters the model should have been able to show a “dynamic aphasic behavior”. As reported in the second Chapter, patient OTM had a similar pattern of performance to patients ANG and CH (Robinson et al., 1998; Robinson et al., 2005) on the sentence completion task. OTM performed almost at ceiling with the high response predictability sentences while performing much worse (50% of accuracy; most of the errors being omissions) when given the other kind of sentence (i.e. low response predictability). The model succeeded to reproduce OTM’s behaviour when the lateral parameter was fixed at “its normal value” of 0.205 but the self parameter was lowered to the value of 0.745 (see table 3.1). Following a procedure similar to that used by Cooper and Shallice (2000), any trial that was not completed (i.e. in which no speech act reached the threshold value of 0.8) within 3600 cycles— about 4 times the normal task completion time—was aborted. Figure 3.4 shows that, in the dynamic aphasia simulation, the low response predictability sentences are completed significantly less often than the other kind of sentences (i.e. accuracy 46 %, 23/50 correct responses, vs. 100% respectively; $\chi 2$ (1) = 34.29, P < .001) and also that the former are slower than the high response predictability sentences (Z = -4.13, p < 0.001). When the accuracy performance on the low response predictability sentences is considered, a significant difference between the two simulations was obtained ($\chi 2$ (1) = 27.97, P < .001). However, these sentences were completed only marginally slower in the dynamic aphasic simulation than in the adult subjects simulation (Mann–Whitney *U* = 400, p = 0.062; see figure 3.4).

As shown above, having an appropriate balance between the values of the self and lateral parameters seems to be critical for correct model behaviour. Thus, we tested the hypothesis that the same pattern of impaired performance could be obtained when the lateral parameter is increased (e.g. 0.23) and the self parameter is fixed at its normal value (i.e. 0.77) (see table 3.1). Accordingly, a pattern of impaired performance similar to that described above was also obtained in this further series of simulations. The model was indeed faster at completing high than low response predictability sentences (Z = - 3.36, p < 0.002) and also more accurate with the former relative to the latter kind of sentences (100% accuracy vs. 40%, 20/50 correct responses, respectively; $\chi2$ (1) = 40.04, p < .001). Finally, as far as the critical condition of the low response predictability sentences is concerned, no differences between the two simulations of dynamic aphasia were found for this condition both for response time (Mann–Whitney U = 185, p = 0.27) and accuracy data ($\chi2$ (1) = .163, P = .68). Furthermore, the high response predictability sentences were also associated to very similar response times (161 and 164 cycles) in the two simulations of dynamic aphasia.

As a graphical example of our IAN behavior, figure 3.5 illustrates some attempts made by the network to select a speech act intention in order to complete a low response predictability sentence. The left part of the figure (i.e. A) shows the activation of nodes for the adult subjects simulation during one trial made on the sentence *The children were...*. The right part (i.e. B) shows an attempt to complete the same sentence made by the model during the simulation of dynamic aphasia. As shown by the figure, a speech act is successfully selected (activation above threshold) in the adult subjects simulation but not in the dynamic aphasia simulation.

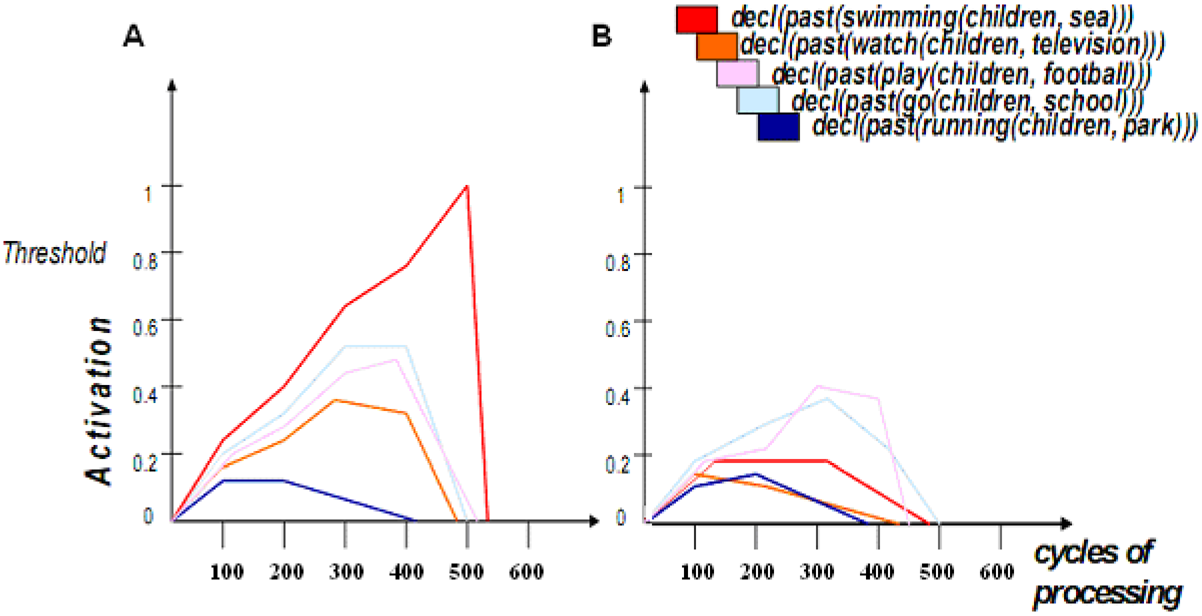

Figure 3.5: Activation values of speech act intentions in the interactive activation network. The sentence to be completed in this example is *The children were…*. On the left (A) an example of the network used in the normal adults simulation is illustrated. Here, the fact about *children swimming* is selected as speech act intention after about 450 cycles. The right part of the figure (B) illustrates a failed attempt to complete the same sentence in the dynamic aphasia simulation.

3.6. General discussion

In this chapter we have presented a computational model of the sentence completion task. The model was developed within the COGENT information processing package (Cooper, 2002) following the detailed lines of the DOMINO framework (Fox & Das, 2000). The complexity of the processes that operate at the level of conceptual preparation of language production suggests that an initial model will be necessarily a substantial simplification of the processes addressed. Our model focused on some of the macroplanning processes of language production, namely those of the generation of communicative intentions and the selection of information for expression. As already shown, the output of macroplanning is a series of speech act intentions and in our model these represent the candidate ways in which a given sentence could be completed.

We focused on the simplified domain of sentence completion that, although being a complex task, constrains the kinds of possible speech acts that could be encoded. We implemented the informative and request speech acts. This choice was also motivated by the aim of making the first attempt to model dynamic aphasia. In order to reproduce and explain the pattern of performance that patient OTM showed in the sentence completion task we provided the model with both low and high response predictability sentences. We predicted that the model would show worse performance (both in accuracy and processing cycles) with the former than the latter kind of sentences.

The macroplanning model dealt mainly with processes that are typical SAS processes (e.g. goal generation, strategy generation and evaluation, plan construction; see Norman & Shallice, 1980; 1986); however a rudimentary way to deal with CS was also included in the model. Indeed several speech act intentions competed with each other for selection in an IAN. The way in which competition operates in the network is similar, although grossly simplified, to the way in which different action schemas competed in the Cooper and Shallice' (2000) model of control of routine actions (see also Cooper's model, 2002, of the WCST for similar mechanisms of competition between different schemas of sorting strategies). In the model we have exploited the dynamics of this kind of interactive activation network in the attempt to simulate patient OTM's problems with low response predictability sentences. Thus we assumed, as done in previous cases of dynamic aphasia (Robinson et al., 1998, 2005; Warren et al., 2003), that the main problem in this syndrome is in the selection of responses when many alternative options are activated by a stimulus (i.e. low response predictability sentences) rather than in the process of setting communicative goals.

Patient OTM's performance was successfully simulated when the self activation and lateral inhibition parameters of the IAN network were manipulated. In more detail, the model required more cycles and was less accurate in completing low than high response predictability sentences when the self activation parameter was lowered or the lateral inhibition parameter increased relative to the values that were employed in the normal subjects' simulation.

As we have briefly reported in section 3.5.1, Cooper and Shallice (2000) showed that some aspects of certain neuropsychological conditions (e.g. bradykinesia in Parkinson's disease) can be modelled by manipulating the parameters of an IAN. They claimed that certain relationships exist between parameter values and neurological correlates which underlie these pathological conditions. For instance, they proposed that the *Lateral:Self parameter* of their model, which controlled the proportion of self and lateral influence on the final influence on a node activation, could correlate with the level of dopamine. In more detail, they showed that a reduction to this parameter, thereby decreasing the activation of schemas in their network, caused the model to produce a behaviour similar to bradykinesia (e.g. slowed initiation of willed action), which is a specific feature of patients who suffer from Parkinson's disease (a condition characterized by a strong depletion of dopamine in the BG; see Introduction and Chapter 4). Moreover, the authors found that bradykinesia was reduced when a specific action was constrained by the stimulus thus leading to little competition between alternatives. More specifically, in the model of Cooper and Shallice, bradykinesia occurs if several competing action schemas, with similar activation values, are present at the beginning of the task. Under these situations self influence is considered to play an important role since it can separate competing schemas; a reduction in this parameter in fact leads to a general slowing in competition.

The simulation results on patient OTM are clearly in line with the idea that an incorrect balance between the self and lateral parameters of an IAN can lead to poor performance particularly in situations of high competition. Direct evidence supporting our argument comes also from previous accounts of dynamic aphasia. Within the domain of language production, the account that Robinson et al. (1998) proposed for their patient ANG was focused on the idea that activated verbal alternatives compete with each other through mutual inhibition. The greater the number of competing verbal responses, the greater the amount of inhibition each response receives from its competitors. Thus, in situations of many verbal responses activated, there should be a lower probability for one response option to become dominant. In a similar fashion, Robinson et al., (2005) interpreted the deficit of patient CH as due to an impairment in conceptual preparation which was particularly present when many competing verbal response options are activated by a stimulus.

In the Introduction of the thesis we briefly discussed as selection of task-relevant responses can occur through either an accentuation of relevant responses or the inhibition of irrelevant information. We also reported evidence (Gazzaniga et al., 2002; Mostofsky & Simmonds, 2008) that the two mechanisms are similar in nature both possibly depending on fronto-striatal circuits. The present simulation, and more generally our model, supports the idea that in an interactive activation process both the parameters of self activation and lateral inhibition are important in the selection of task-relevant responses. Thus, our simulation also suggests that OTM's language output disorder may be due to a decreased activation of verbal responses in situations of high competition. Furthermore, the lesion involving the BG of patient OTM also indicates that these structures are important for self-activation of schemas and more generally for the selection of task-relevant responses (Robbins & Sahakian, 1983; Norman & Shallice, 1986; Crosson et al., 2003; Copland, 2003).

Finally, although being a grossly simplified model, the embedding of the macroplanning processes within the DOMINO framework provides an additional demonstration of the suitability of this framework for modelling cognitive tasks which involve many SAS and CS processes operating together.

Chapter 4

4.1. Empirical background and aim of the noun and verb generation study in Parkinson's disease (PD) patients

As already shown in chapter 2, fronto-striatal circuits play an important role in verbal response selection; nonetheless our single case analysis supports the idea that subcortical lesions which cause dynamic aphasia also lead to deficits to domains other than language, such as executive function. In this chapter we further investigated the way in which the executive system handles the processes of retrieving and selecting task-relevant verbal responses. In particular, Parkinson's disease (PD) is used as a model for exploring the cognitive functions of the basal ganglia, as done by many others researchers (e.g., Ullman et al., 1997; Longworth et al., 2005). Admittedly, this procedure requires that one bears in mind that any assumption that cognitive deficits in PD patients reflect striatal dysfunction should be made cautiously, given that, for instance, various frontal regions are affected by the degeneration of nigrostriatal and mesocortical dopaminergic pathways which are involved in PD (e.g. Saint-Cyr, 2003; Owen, 2004).

In the study presented in this chapter we have investigated noun and verb generation in populations of PD patients and healthy older subjects. As briefly discussed in the Introduction, behavioral and neuroimaging studies have used the verb generation task as a probe for exploring the mechanisms and neural substrates involved in the retrieval and selection of semantic and syntactic knowledge (Petersen, Fox, Posner, Mintun, & Raichle, 1988; 1989; Petersen, Fox, Snyder, & Raichle, 1990; see also Martin & Cheng, 2006). This task requires participants to produce a verb in response to a noun stimulus and several factors are likely to play a role in determining optimal performance. For instance, the speed and accuracy of word generation may depend both on the number of possible responses (response selection) and on the strength of association between cues and responses (associative strength). In our study we have exploited a paradigm of verb generation that Martin and Cheng (2006; see also Martin & Byrne, 2006) have recently proposed in order to consider whether strength of stimulus-response associative links, rather than selection demands (e.g. Thompson-Schill et al., 1997; 1998; see also section 1.3 of the Introduction), is the critical factor that explains performance on the verb generation task.

In more detail, Thompson-Schill et al. (1997; 1998) have provided evidence that indicates that the critical process in verb generation is the selection among potential responses. Thompson-Schill et al. (1997) investigated the production of verbs in conditions of low or high selection (i.e., when either one verb -*apple* → *eat*- or at least two verbs -*map* → *travel, find*- are typically elicited by the noun stimulus, respectively). They found higher RTs and an increased activation of the left inferior frontal gyrus (LIFG) in the high selection condition. Following up their study, Thompson-Schill et al. (1998) have also shown that lesions to the LIFG were associated with difficulties in producing verbs in the high selection condition, suggesting that LIFG is involved in response selection from amongst competing alternatives. Martin and Cheng (2006) have, however, observed that associative strength and selection demands were confounded in Thompson-Schill et al's studies. They claimed that the two conditions that differed in selection demands in Thompson-Schill et al.'s paradigm, also differed in association strength, whereby the condition with high selection demands was also of weaker association than the condition with low selection demands. In order to resolve this potential confound, Martin and Cheng compared three experimental conditions: (1) strong association-high selection, (2) strong association-low selection, and (3) weak association-high selection. In the strong association conditions, either one verb (low selection) or two verbs (high selection) were strongly associated with the noun stimuli, while in the weak association condition the stimulus-response associative strength was much weaker. These authors proposed that strong stimulus-response associative strength drives automatic retrieval, and controlled search processes are activated only when automatic retrieval fails, that is, in situations of weak stimulus-response associative strength. Martin and Cheng (2006) found no effect of selection demands (i.e. condition 1 vs. condition 2) in a patient with LIFG damage and in two samples of young and older controls. Participants' RTs were instead affected by the strength of association between the noun stimulus and the most frequently produced verb. This evidence led Martin and Cheng (2006) to conclude that the LIFG is involved in semantic controlled retrieval rather than in selection of responses between alternative options.

Previous studies have found that PD patients are impaired with verbs while performing in the normal range with nouns (Péran et al., 2003). A common interpretation for this pattern of results has been that to consider verbs as a lexical category that can be the focus of a specific deficit in PD patients; this would be based on evidence which shows that verb processing involves the operation of the prefrontal cortex, while noun processing involves more posterior brain regions (Perani et al., 1999; Shapiro, Pascual-Leone, Mottaghy, Gangitano, & Caramazza, 2001; Shapiro, Moo, & Caramazza, 2006). Previous studies on PD patients and verb/noun generation, however, have not investigated aspects of selection demands and association strength (but see Castner et al., 2008). The present study aims to fill this gap by trying to give a better functional description of the tasks employed. We will argue that the factors of association strength and selection demands influence the ability of PD patients to produce verbs (and nouns) and that the results help to better understand how fronto-striatal circuits contribute to response retrieval and selection. As briefly shown in the Introduction, previous evidence has suggested that BG play a role in response selection and inhibition (Longworth et al., 2005) and, more generally, in the controlled processes of lexical retrieval (Crosson et al., 2003; Persson et al., 2004; Copland, 2003). Thus in our study we expected PD patients to have in general more problems with verbs than nouns (Péran et al., 2003) but also to show a non-uniform pattern of performance across the different conditions of the verb generation task. The greatest difficulties should in fact manifest in the conditions with high selection demands and even more in that with weak associative strength.

In line with the expectations our investigation has shown that both factors of response selection and associative strength are important for verb and noun production with the latter having a greater impact on performance; and also that the most critical condition for PD patients is the condition of verb generation with weak stimulus-response associative links. More generally, the findings of this study support those obtained in the patient OTM and they together suggest that BG have a non-language specific role in the supervisory processes required during lexical retrieval.

Before describing the noun and verb generation experiment, a succinct picture of the pathophysiology of PD is given in the section below.

4.2. Parkinson’s disease: anatomo-functional considerations

PD belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells. The four primary symptoms of PD are *a) tremor*, or trembling in hands, arms, legs, jaw, and face; *b) rigidity*, or stiffness of the limbs and trunk; *c) bradykinesia*, or slowness of initiating movement; and *d) postural instability*, or impaired balance and coordination. PD is also called “primary Parkinsonism” or “idiopathic PD”; it usually affects people over the age of 50. Early symptoms of this disease are subtle and occur gradually. In some people the disease progresses more quickly than in others. As the disease progresses, the shaking, or tremor, which affects the majority of PD patients may begin to interfere with daily activities. Other symptoms may include depression and other emotional changes, as well as difficulty in swallowing and chewing. The prevalence of PD in industrialised countries is estimated at 0.3% of the general population and about 1% of the population older than age 60 years (Samii, Nutt, & Ransom, 2004).

As briefly reported in the Introduction, the underlying pathological finding in PD is degeneration of the dopaminergic projections from the susbstantia nigra pars compacta to the caudate nucleus and putamen (striatum). The depletion of dopamine in the striatum has serious consequences on the fronto-striatal circuitry. As main effects one observes an enhanced excitation of the subthalamic nucleus and the globus pallidus internus which causes an increased inhibition of the thalamus (Saint-Cyr, 2003; Postuma & Dagher, 2006). Figure 4.1 shows both the normal functional anatomy of the BG and the pathological anatomy which is characteristic of people affected by PD. Clinical signs of PD are evident when about 80% of striatal dopamine and 50% of nigral neurons are lost (Fearnley & Lees, 1991).

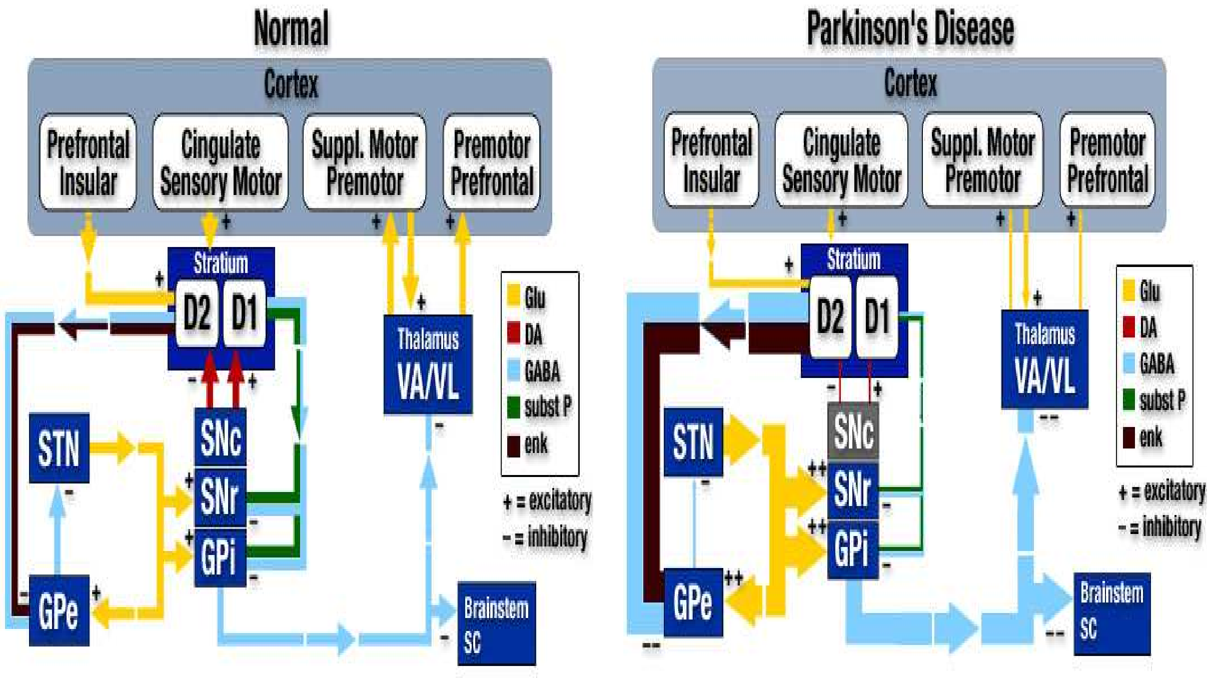

Figure 4.1: Normal functional anatomy of the basal ganglia is shown in the left part of the figure; pathological functional anatomy of the basal ganglia in Parkinson’s disease is shown in the right part of the figure. GPi, globus pallidus interna; GPe, globus pallidus externa; SNr,substantia nigra pars reticulata; SNc, substantia nigra pars compacta; STN subthalamic nucleus; VL, ventrolateral; VA,ventroanterior; D2 and D1, dopamine striatal receptors; Glu, Glutamate, DA dopamine; subst P, substance P; enk, enkephalin. (picture taken from the *Movement Disorder Virtual University*; http://www.mdvu.org/library/disease/pd/par_path.asp).

Studies of patients with PD suggest that the characteristic clinical symptoms of bradykinesia, tremor, and rigidity are frequently accompanied by impairments in cognitive functions. Between 15 and 20% of PD patients develop dementia (Lewis, Dove, Robbins, Barker, & Owen 2003; Owen, 2004). However, a less severe cognitive impairment is a well recognized feature of the disease and several cognitive deficits can also be observed in nondemented PD patients at the early stages of the disease (Péran et al., 2003; Owen, 2004). Often, the pattern of cognitive impairments observed in the early stages of PD resembles that produced by frontal-lobe damage including deficits in executive functions such as planning and problem solving (e.g. Owen et al., 1998), working memory (e.g. Lewis et al., 2005), set shifting (e.g. Cools, Barker, Sahakian, & Robbins, 2001), and response inhibition (Bouquet et al., 2003; Castner et al., 2007). This executive dysfunction in PD has been shown to be extremely sensitive to the effects of controlled L-dopa withdrawal, suggesting a predominantly dopaminergic substrate for the deficits observed (Lewis et al., 2003; Owen, 2004).

4.3. Materials and Methods of the study

4.3.1 PD patients and Control Subjects

Twenty right-handed Italian PD patients (12 males and 8 females) were included in the study. The diagnosis of idiopathic PD was established by a neurologist in accordance to the clinical criteria of the United Kingdom Parkinson’s disease Society Brain Bank (UK-PDS-BB; Gibb & Lees, 1988). The patients were consecutive referral to the Department of Physical Medicine of the “Gervasutta” Rehabilitation Hospital, Udine, for a standardized neuropsychological examination.

All patients were in the mild to moderate stages of the disease, with scores on the Hoehn and Yahr’s scale (Hoehn & Yahr, 1967) that ranged from one to three. Patients’ motor disability was also evaluated using the motor part of the Unified Parkinson’s disease Rating Scale (UPDRS; Fahn et al., 1987). Patients were screened for dementia using the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh 1975) and those with a score below 24 were excluded from the study. PD patients were also screened for depression, and we excluded those with scores > 10 on the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). All patients were on antiparkinsonian medication, 16 were receiving L-dopa and 17 were taking dopamine agonists. Some of the patients were also taking monoamine-oxidase-B-inhibitors (three patients), catechol-O-methyltransferase inhibitors (two), amantadine (one), antidepressants (two), atypical antipsychotics (two) and benzodiazepine (one). All patients were tested in the ‘on’ medication state. Patients with atypical parkinsonism, vascular parkinsonism, drug-induced parkinsonism, and those with parkinsonism following dementia were excluded from the study.

A control group of 20 right-handed Italian subjects, closely matched to the PD patients for age, sex, education, and MMSE scores took part in the study as well. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and was previously approved by SISSA ethical committee. Demographic and clinical data of PD patients and control subjects are summarized in Table 4.1.

Table 4.1.

Demographic and clinical data of PD patients and control subjects (mean ± SD).

Parameter	PD patients (N=20)	Older controls (N=20)
Age (years)	64.6 ± 5.9	66.1 ± 7.4
Education	7.45 ± 3.2	8.8 ± 4.03
Sex (M/F)	12/8	12/8
Age at Onset (years)	57.8 ± 6.4	
Duration of illness (years)	7.4 ± 4.9	---
Hoehn and Yahr score:		---
Stage I	n = 2	---
Stage II	n = 14	---
Stage III	n = 4	---
UPDRS motor score	17.1 ± 9.7	---
MMSE	28.4 ± 1.1	28.7 ± 0.9
BDI	7.4 ± 2.5	---
Dopamine agonist mg/day (range)		---
Pramipexole	1.97 ± 0.45 (n=12; 0.45 - 2.1)	---
Ropinirole	17 ± 3.5 (n=3; 15 - 21)	---
Cabergoline	2.8 ± 1.1 (n=5; 2 - 4)	---
Levodopa mg/day (range)	503.1 ± 283.7 (n=16; 100 - 1150)	---

Notes. Values are expressed as mean ± SD; UPDRS = Unified Parkinson’s disease Rating Scale (Fahn, Elton, & Members of the UPDRS Development Committee, 1987); MMSE = Mini Mental Status Examination (Folstein, Folstein, & McHugh, 1975); BDI = Beck’s Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).

4.3.2 Neuropsychological measures

Neuropsychological assessment took place during two different testing sessions with a gap of one week between the two sessions. At the beginning of the second testing session the experimental task was administered. The neuropsychological battery was as follows: overall cognitive functions were assessed using Coloured Progressive Matrices (CPM; Lezak, 1995). Memory functions were assessed by means of a Story Free Recall Test, immediate and delayed versions (from Esame Neuropsicologico Breve, ENB, Mondini, Mapelli, Vestri, & Bisiacchi, 2003), the Forward Digit Span (Lezak, 1995), and the Corsi Block-tapping Test (Lezak, 1995). Construction ability was assessed using a Figure Copy Test (from Batteria Deterioramento Mentale, BDM, Caltagirone et al., 1995). Frontal lobe functions were assessed using the Wisconsin Card Sorting Test (WCST, Heaton, Chelune, Talley, Kay, & Curtiss, 1993), the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997), the Similarities subtest of the WAIS-R (Wechsler, 1981), a Letter Fluency Test (Lezak, 1995), the Clock Drawing Test (Lezak, 1995), the Cognitive Estimation Test (ENB, Mondini et al., 2003), the Trial Making Test A and Trail Making Test B (Lezak, 1995), the Stroop Colour Word Test (Lezak, 1995), and the Frontal Assessment Battery (FAB, Dubois, Slachevsky, Litvan, & Pillon, 2000). The latter battery consists of six subtests exploring the following: conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy.

Normative data provided in test manuals were used for all the ENB subtests (Mondini et al., 2003), for all the BDM subtests (Caltagirone et al., 1995) and for the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997). Normative data for other tests were as follows: for Coloured Progressive Matrices and Letter Fluency Test we used those provided by Caltagirone et al. (1995); for the Forward Digit Span, the Trail Making Test A and B, and the Clock Drawing Test we used those provided by Mondini et al. (2003); for the Stroop Colour Word Test those provided by Barbarotto et al.(1998); for the Corsi Block-tapping Test those provided by Spinnler and Tognoni (1987); for the Similarities subtest of the WAIS-R those provided by Orsini and Laicardi (2001); for the FAB those provided by Dubois et al. (2000); and for the WCST those provided by Hardoy, Carta, Hardoy, and Cabras (2000). A test score was categorized as impaired if it was below age-appropriate cut-off (when these were available) or the fifth percentile of the normative sample. The percentage of patients which obtained impaired and unimpaired test scores was computed for each measure (see table 4.2).

PD patients had the greatest impairments on the WCST test (9/20 of the patients were impaired on the number of categories recognized), on the FAB battery (12/20 patients impaired), and on the Brixton test (13/20 patients impaired); however, only one patient was impaired on the Stroop test and only another one performed outside the normal range on the verbal fluency test.

Table 4.2.

Descriptive statistics for neuropsychological variables and percentage of PD patients impaired on each of them (N=20).

Variable	Mean (SD)	Range	% Patients impaired
Forward digit span	5.2 (1.1)	3 - 7	5
Corsi Block-tapping test	5.6 (1.1)	4 - 7	0
Story free recall test, immediate	9 (4.1)	3 - 17	30
Story free recall test, delayed	13.8 (4.2)	7 - 22	10
CPM	26.3 (5.2)	15 - 36	5
Verbal fluency (FAS)	32.7 (15.7)	9 - 68	5
FAB	15.1 (2.4)	10 - 18	60
Stroop CW	17 (6.2)	4 - 34	5
TMT-A	60.5 (55)	21 - 281	5
TMT-B	181.3 (93.8)	65 - 420	25
WAIS-Similarities	13.4 (5.9)	0 - 24	5
WCST-n° categories	2.8 (1.6)	0 - 6	45
WCST-n° errors	58.5 (20.1)	14 - 93	15
WCST-n° perseverative errors	33.9 (17)	7 - 79	15
WCST-n° non perseverative errors	24.6 (9.7)	6 - 40	35
Brixton	25.7 (8.2)	6 - 45	65
Cognitive estimation test	4.7 (0.5)	4 - 5	0
Clock Drawing Test	7.8 (3)	0 - 10	15
Figure Copy Test	8.3 (1.9)	4 - 10	20

4.3.3 Stimuli

Verb production task

Three hundred and thirty (di- and trisyllabic) nouns were selected from the "*Veli Dictionary of Frequency for Italian Spoken Language*" and administered to 46 Italian subjects (range 20-57 years-old). Subjects were asked to provide a related verb for each noun. They were also asked to provide a judgment of concreteness on a five-point scale for each noun. A ratio of the response frequency of the most common response to the response frequency of the second-most common response was calculated for each noun as a measure of selection demand (see Thompson-Schill et al., 1998) (see next subsection for a minor modification used). A measure of stimulus-response association strength was also calculated for each noun. The response frequency of a verb was used as an index of its association strength with the stimulus noun. The association strength for each noun was given by the ratio of the mean association of the first two most common responses to the number of subjects who judged noun-verb stimuli (see Martin & Cheng, 2006).

On the basis of these data, nouns were chosen for three conditions: Low selection-Strong association (LS-SA; e.g. the noun *lattina* (*can) → bere* (*to drink*) in 25 out of 46 subjects and *stappare* (*to broach*) in 4 out of 46 subjects), High selection-Strong association (HS-SA; e.g. the noun *lampada (lamp)* elicited in 21 subjects *accendere* (*to turn on*) and in 17 subjects *illuminare* (*to light on)*), and High selection-Weak association (HS-WA; e.g. the noun *spada* (*sword*) elicited in 8 subjects *combattere* (*to fight*) and in 8 subjects *ferire* (*to wound)*). Twenty-seven nouns were selected for each condition; in each of these four stimuli were used as practice items only. A one-way ANOVA showed that there were no significant differences between the frequency and the concreteness of the word nouns that were used in the three conditions of the task (F (2, 68) = 0.186, p = 0.83 for frequency, and F (2, 68) = 0.42, p = 0.655 for concreteness).

The nouns in the Low-Selection condition had a selection ratio of 15.2 on average whereas those in the two high selection conditions had a ratio of 1.36 on average for HS-WA and 1.55 on average for HS-SA. A one-way ANOVA showed differences in selection demands across the three conditions (F (2, 68) = 85.73, p < 0.001). Bonferroni post–hoc tests for multiple comparisons showed that no difference was present between HS-SA and HS-WA while differences between these two high selection conditions and the low selection condition were present (p < 0.001 for both comparisons). The nouns in the strong-association conditions had a mean ratio of association strength of 0.39 for LS-SA, and 0.38 for HS-SA whereas the nouns in the weak association condition (HS-WA) had a mean ratio of association strength of 0.13. A one-way ANOVA showed differences in association strength between the three conditions of the task (F (2, 68) = 298.61, p < 0.001). Bonferroni post–hoc tests for multiple comparisons showed that no difference was present between LS-SA and HS-SA while differences were present between HS-WA and HS-SA and between HS-WA and LS-SA (p < 0.001 for both comparisons, see table 4.3).

Noun production task

The same 330 nouns were given to another sample of 29 Italian subjects (range 21-55 years-old). This time they were requested to provide another associated noun for each noun stimulus. Measures of selection demands and ratios of association strength were calculated for each stimulus in the same manner as for the verb generation task. One-way ANOVAs were run for both measures. The first of these showed that the two strong association conditions (LS-SA and HS-SA) were matched for association strength and that each of these conditions differed from the weak association condition HS-WA (p < 0.001 for both comparisons). The second one-way ANOVA showed that the two high selection conditions were matched for selection demands while they differed from the low selection condition ($p < 0.001$ for both comparisons, see table 4.3). Two others one-way ANOVAs also showed that noun stimuli in the noun production task did not differ either in frequency ($F(2, 68) = 0.004$, $p = 0.996$) or in concreteness ($F(2, 68) = 0.44$, $p = 0.643$). In a similar way to the verb production task, twenty-seven nouns were selected for each condition of the noun production task; in each of these four nouns served as practice items.

Noun stimuli were also matched across the two tasks for both concreteness ($F(1, 137) = 0.002$, $p = 0.96$) and frequency ($F(1, 137) = 0.39$, $p = 0.84$). Moreover, the mean selection demands of the stimulus nouns of the four high selection conditions (i.e. two conditions for each task) varied between 1.36 and 1.61 (see table 4.3) with no significant differences across conditions. The two conditions with low selection demands were also matched for this measure (for the noun-verb stimuli if the second highest response has a value 1, which is in practice the floor value, then the selection value in all cases (44, 41, 37 and 30) exceeds the maximum possible with the noun-noun stimuli where the maximum value is 28. For the four values concerned the first response frequency value was reduced to 0.63 of its measured value, 0.63 being the ratio of the number of subjects who judged noun-noun stimuli to those who judged noun-verb ones).

The two tasks were also matched for the ratios of association strength, both when the two HS-WA conditions were concerned (the mean ratio of association strength was equal to 0.13 for the HS-WA condition of verb production and equal to 0.14 for the relative condition of noun generation) and when the conditions with strong associations were considered (the mean ratios of association strength varied between 0.37 and 0.39 in these four conditions with no significant differences between them; see table 4.3).

Table 4.3
Mean values of Selection Demands and Association Strength for each condition of the two tasks

	LS-SA		HS-WA		HS-SA	
	SELECTION DEMANDS	*ASSOCIATION STRENGTH*	*SELECTION DEMANDS*	*ASSOCIATION STRENGTH*	*SELECTION DEMANDS*	*ASSOCIATION STRENGTH*
NOUN-VERB	15.2 (3.97)	0.39 (0.057)	1.36 (0.27)	0.13 (0.03)	1.55 (0.44)	0.38 (0.04)
NOUN-NOUN	11.9 (6.83)	0.37 (0.07)	1.41 (0.28)	0.14 (0.02)	1.61 (0.45)	0.37 (0.05)

Notes: Norms for verb production have been calculated on 46 young subjects while those for noun production have been calculated on a sample of 29 young subjects. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Standard Deviation is reported in parentheses. See text for more details.

Task-relevant response ratio

We calculated Task-Relevant Response (TRR) ratios in order to give a quantitative evaluation of the intrinsic difficulty of the three different conditions of the two tasks. Forty-five normal subjects (range 24-55 years old) were asked to provide the first word that came to mind (e.g. verbs, adjectives, nouns) for each stimulus noun used in the two experimental tasks. Proportions of TRR were obtained for each stimulus noun (see figure 4.2). For the verb generation task, ratios of TRR were given by the number of verbs (task-relevant responses) produced for a given noun divided by the total number of responses (e.g. verbs, adjectives and nouns). Kruskal-Wallis tests showed significant differences between the proportions of verbs produced for the three conditions of the verb production task (Chi Square (2) = 18.34, $p < 0.001$). Post hoc pair-wise contrasts made across conditions (with Bonferroni correction for multiple comparisons applied) did not show significant difference between stimulus nouns of the LS-SA condition (that were followed on average by 11% of verbs), and stimuli of the HS-SA condition (followed by 7.8% of verbs; Mann Whitney U = 182.5, $p = 0.07$). By contrast, the stimuli used in the HS-WA condition were followed by significantly less verbs (2.77%) than those used in both the LS-SA (Mann Whitney U = 83, $p < 0.001$) and HS-SA conditions (Mann Whitney U = 138, $p < 0.006$).

Proportions of TRR were also obtained in an analogous fashion for the nouns used as stimuli in the noun production task. Since 80% of the responses to the entire set of noun stimuli were other nouns, the proportions of TRR in the noun production task were much higher than those in the verb production task (see figure 4.2). Again, Kruskal-Wallis tests showed significant differences in the proportions of TRR produced for the three conditions of the noun production task (Chi Square (2) = 10.82, $p < 0.005$). Post hoc pair-wise contrast made across conditions (with Bonferroni correction for multiple comparisons applied) showed that stimulus nouns of the HS-WA condition were less often followed by noun responses (73.3 % of responses) than nouns of both LS-SA (83.2% of nouns; Mann Whitney U = 154 uncorrected $p = 0.015$) and HS-SA conditions (85.6%; Mann Whitney U = 121, $p < 0.003$). Finally, there was no difference between proportion of nouns produced as response to stimuli of the LS-SA and HS-SA conditions of the noun generation task (Mann Whitney U = 242, $p = 0.62$).

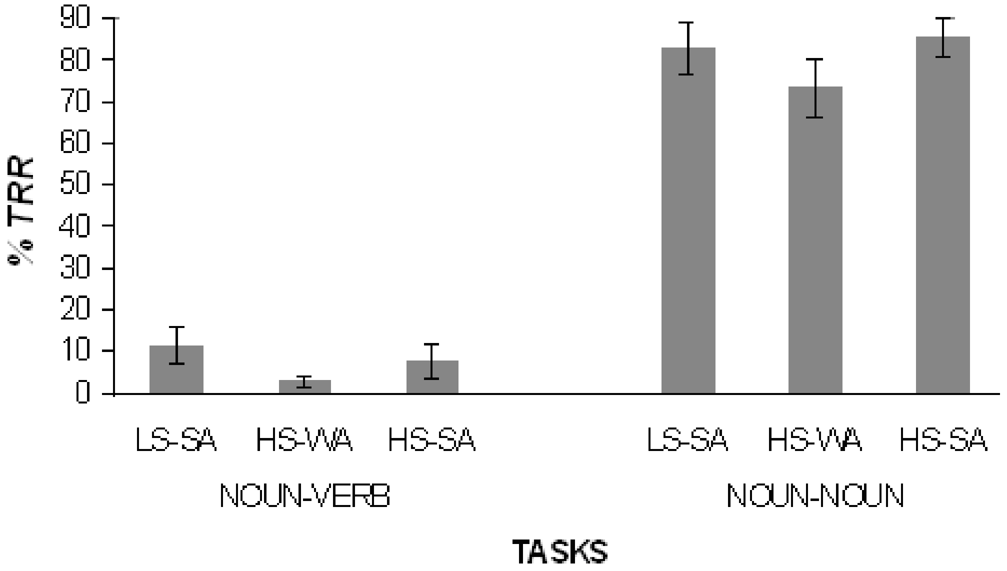

Figure 4.2: Percentages of Task-Relevant Response (TRR) for each condition of the tasks. The x-axis reports the conditions of both tasks while in the y-axis values of TRR are reported for each condition. Measures of TRR are obtained using free association norms from noun stimuli used in the two experimental tasks. Bars indicate standard deviation. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. See text for more details.

4.3.4. Procedure

The two tasks were presented in two blocks one after the other. The order of blocks was counterbalanced across subjects. On each trial, a noun from one of the three conditions was randomly selected and read to the subjects. Participants were asked to produce a related verb (or a related noun) as quickly as possible. Responses and onset latencies were recorded. Following Péran et al. (2003), the task had to be performed within a period of 4 seconds for older subjects and of 6 seconds for PD patients. These authors argue that giving PD patients 2 extra seconds could compensate for the slow articulatory rate that is often present in PD.

4.3.5. Data analysis

Data from older controls and PD patients were compared using both analyses of variance with repeated measures and post-hoc contrasts with task and group as factors (considering performance either as accuracy or reaction times). Analyses of covariance were carried out for both tasks on the number of errors made by PD patients using TRR as covariate and stimulus condition as fixed factor. Non-parametric analyses were used to analyse error type profiles across subject populations. Non parametric correlations were used to assess the relationship between the performance of PD patients in both generative tasks and the neuropsychological measures and TRR ratios (the same analyses were carried out also for older subjects where possible).

4.4. Results

4.4.1. Older subjects vs. PD patients: Accuracy analyses

The performance of PD patients and of older subjects is shown in figure 4.3. An arcsine transformation was performed on proportions as the error data would be binomially distributed. Following the transformation, data for each group did not violate assumptions of normality, as indicated by the Shapiro-Wilks results.

A three-factor 2x2x3 repeated measures ANOVA with the factor of group (Older and PD subjects) as between subjects factor and the factors of task (Noun and Verb production) and condition (LS-SA; HS-WA; HS-SA) as within subjects factors was performed. The analysis showed a significant main effect of group ($F(1, 38) = 7.42$, $p < 0.02$), a main effect of task ($F (1, 38) = 30.74$, $p < 0.001$), a main effect of condition ($F (2, 76) = 85.92$, $p < 0.001$), a two-factor taskXgroup interaction ($F (1, 38) = 32.98$, $p < 0.001$), a two-factor conditionXgroup interaction ($F (2, 76) = 7.71$, $p < 0.003$), and a two-factor taskXcondition interaction ($F (2, 76) = 54.42$, $p < 0.001$). However the three-factor taskXconditionXgroup interaction ($F (2, 76) = 0.594$, $p = 0.534$) was not significant.

In view of the taskXgroup interaction, each task was divided into its three conditions and analysed separately. A 2x3 repeated measures groupXcondition ANOVA was conducted for the noun production task. The analysis showed a significant main effect of condition ($F (2, 76) = 6.38$, $p < 0.04$) but not a significant main effect of group ($F (1, 38) = 0.003$, $p = 0.95$). The two-factor groupXcondition interaction was significant ($F (2, 76) = 3.58$, $p < 0.04$). In view of the interaction two repeated measure ANOVAs were carried out; the performance on the three conditions of the noun generation task (LS-SA; HS-WA; HS-SA) was analysed separately within each group. These analyses gave a significant main effect of condition for the PD patients ($p < 0.001$) but the same effect was not present for older controls ($p = 0.79$). Post-hoc pair-wise contrasts executed in the PD group showed significant differences (using Bonferroni corrections) for comparisons between LS-SA and HS-WA (uncorrected $p < 0.001$) and for HS-SA vs. HS-WA (uncorrected $p < 0.005$) but no difference was found for the third comparison (LS-SA vs. HS-SA, $p = 0.38$). These results show a clear effect of association strength for PD patients in the noun production task indicating that strong associations between stimuli and responses led to better performance than weak levels of association.

A similar 2x3 repeated measures groupXcondition ANOVA was conducted for the task of verb production. The analysis showed significant main effects of both condition ($F(2, 76) = 107.29$, $p < 0.001$), and group ($F(1, 38) = 19.43$, $p < 0.001$) and also a significant two-factor conditionXgroup interaction ($F(2, 76) = 5.16$, $p < 0.02$). In view of the interaction, two repeated measures ANOVAs were run one for each group. These analyses gave significant main effects of condition for both older controls ($F(2, 38) = 26.30$; $p< 0.001$) and PD patients ($F(2, 38) = 105.49$; $p< 0.001$). Post-hoc pair-wise contrasts in PD patients (using Bonferroni corrections) showed that accuracy was different across all three conditions of verb production, (LS-SA vs. HS-SA, uncorrected $p < 0.01$; LS-SA vs. HS-WA, uncorrected $p < 0.001$ and HS-WA vs. HS-SA, uncorrected $p < 0.001$). Thus in PD patients there were an effect of selection demands together with a stronger effect of association strength (see figure 4.3). Post-hoc pair-wise contrasts in older subjects showed significant differences (Bonferroni corrections applied) in accuracy between LS-SA and HS-WA (uncorrected $p < 0.001$) and between HS-WA and HS-SA, (uncorrected $p < 0.001$). Differently from PD patients, older controls performed at similar levels of accuracy the LS-SA and HS-SA conditions of verb production ($p = 0.21$). This indicates the presence of only an effect of association strength in the accuracy data of verb generation for older controls.

In view of the main effect of Group as well as of the two-factor interaction in the verb generation task, we carried out a series of univariate analysis of variance in order to compare the two groups for performance on each condition of the task. These analyses showed a significant effect of group for each condition of the task (LS-SA: $F(1, 38) = 13.70$, $p < 0.001$; HS-SA: $F(1, 38) = 15.31$, $p < 0.001$; HS-WA $F(1, 38) = 18.72$, $p < 0.001$). Thus PD patients were significantly impaired in all conditions of verb production relative to older subjects.

In order to investigate whether there were between tasks differences in each subject group we performed two 2x3 repeated measures taskXcondition ANOVAs; the first was carried out for PD patients and the second for older controls. The ANOVA made for PD patients showed significant main effects of both task ($F(1, 19) = 39.47$, $p < 0.001$) and condition ($F(2, 38) = 88.92$, $p < 0.001$) and also a significant interaction between the two factors ($F(2, 38) = 41.71$, $p < 0.001$). In view of the interaction post-hoc pair wise contrasts (Bonferroni correction applied) were ran between pair of corresponding conditions of the two tasks. These showed that patients performed significantly poorer in each condition of verb production relative to the conditions of noun production (verb-LS-SA vs. noun-LS-SA, $F(1, 19) = 11.68$, uncorrected $p < 0.004$; verb-HS-SA vs. noun-HS-SA, $F(1, 19) = 14.96$, uncorrected $p < 0.002$; verb-HS-WA vs. noun-HS-WA, $F(1, 19) = 80.74$, uncorrected $p < 0.001$). A similar 2x3 repeated measures taskXcondition ANOVA was carried out for older subjects. The analysis showed the significant main effect of condition ($F(2, 38) = 17.81$, $p < 0.001$) and of the two-factor interaction ($F(2, 38) = 18.14$, $p < 0.001$) but the main effect of task was not significant ($F(1, 19) = 0.051$, $p = 0.82$). In view of the interaction we run post-hoc pair wise contrasts (Bonferroni correction applied) between pair of corresponding conditions of the two tasks. These showed that older controls were significantly less accurate in producing verbs than nouns only in the weak association condition (verb-HS-WA vs. noun-HS-WA, $F(1, 19) = 17.19$, uncorrected $p < 0.002$); by contrast, they performed better with verbs than nouns in the LS-SA condition (verb-LS-SA vs. noun-LS-SA, $F(1, 19) = 8.42$, uncorrected $p < 0.01$) and showed a trend in the same direction in the HS-SA condition (verb-HS-SA vs. noun-HS-SA, $F(1, 19) = 5.99$, corrected $p = 0.024$).

Finally, we also carried out the main statistical analyses on accuracy excluding the correct responses given by the PD patients with latencies between 4 and 6 seconds (so as to have the same deadline, 4 seconds, as control subjects). Following these analyses the main pattern of results with both verb and noun production still held.

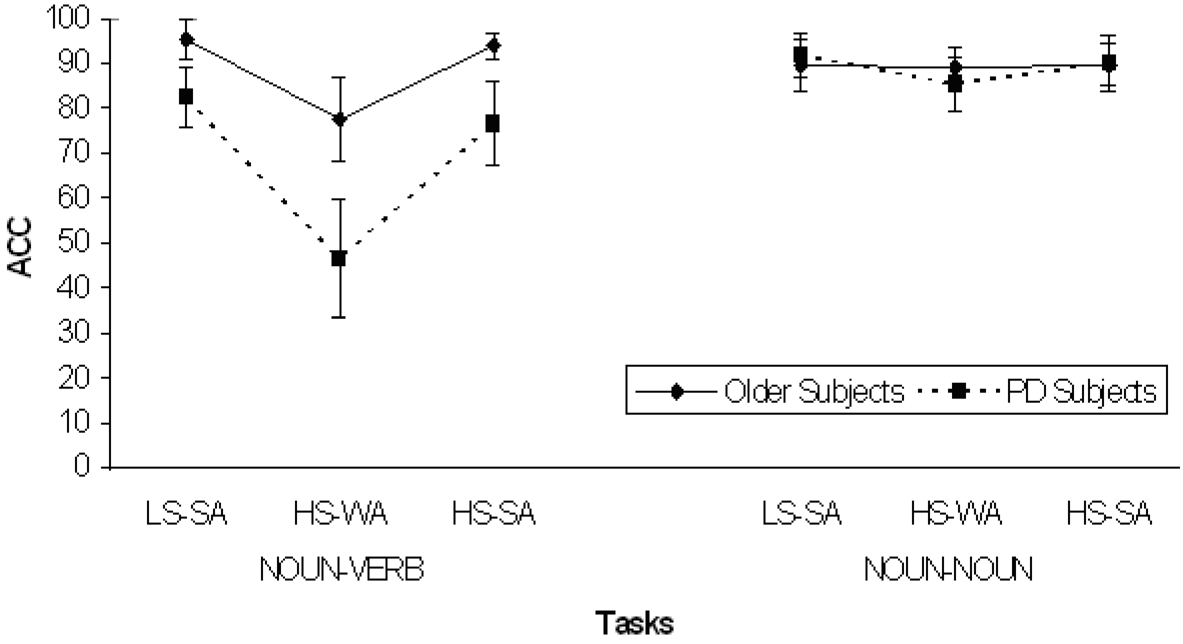

Figure 4.3: Accuracy data for both subject groups in Noun-Verb and Noun-Noun tasks. The x-axis reports the conditions of both tasks while in the y-axis accuracy (ACC) is reported expressed as percentage of correct responses. Bars indicate standard deviation. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association.

4.4.2. Older subjects vs. PD patients: Reaction time analyses

The response times for both groups are shown in figure 4.4. A log transformation was performed on the original data. Following the transformation assumptions of normality were not violated as indicated by the Shapiro-Wilks results.

A three factor 2x2x3 repeated measures ANOVA with the factor of group (Older and PD subjects) as between subjects factor, and the factors of task (Noun and Verb production) and condition (LS-SA; HS-WA;HS-SA) as within subjects factors, was performed. The analysis showed a significant main effect of group (F (1, 38) = 13.53, $p < 0.002$), a non significant main effect of task (F (1, 38) = 2.58, p = 0.11), a main effect of condition (F(2, 76) = 187.24, $p < 0.001$), a two-factor taskXgroup interaction (F (1, 38) = 8.26, $p < 0.008$), a two-factor taskXcondition interaction (F(2, 76) = 57.86, $p < 0.001$), and a trend towards a two-factor conditionXgroup interaction (F(2, 76) = 2.68, p = 0.08). However, the three-factor taskXconditionXgroup interaction (F (2, 76) = 0.393, p = 0.63) was not significant.

In view of the taskXgroup interaction each task was divided into its three conditions and analysed separately. A 2x3 repeated measures groupXcondition ANOVA was conducted for the noun production task. The analysis showed significant main effects of both condition (F

(2, 76) = 15.99, p < 0.001) and group (F (1, 38) = 6.64, p < 0.02), but the two-factor interaction was not significant (p = .542). Even though the interaction was not significant pair-wise comparisons between the levels of the condition factor were made for each group. Older subjects showed significant differences (Bonferroni correction for multiple comparisons applied) only for the comparison made between LS-SA and HS-WA conditions, (F (1, 19) = 10.88, uncorrected p < 0.005). A trend toward a difference between HS-WA and HS-SA (p = 0.073) was also present. No significant difference was found for the comparison made between the conditions LS-SA and HS-SA (p= 0.26). For the PD group, significant differences (Bonferroni correction for multiple comparisons applied) were found for comparisons made between LS-SA vs. HS-WA (F (1, 19) = 17.98, uncorrected p < 0.001) and between HS-SA vs. HS-WA (F (1, 19) = 15.20, uncorrected p < 0.002) but no difference was found for the third comparison (LS-SA vs. HS-SA, p = 0.69). Thus this data show that an effect of association strength was also present in reaction times for the PD patients group in the noun generation task.

A similar 2x3 groupXcondition repeated measures ANOVA was conducted for the task of verb production. The analysis showed significant main effects of condition (F (2, 76) = 204.74, p < 0.001) and group (F (1, 38) = 18.54, p < 0.001) but the interaction was not significant (F (2, 76) = 2.17, p = 0.12). Even though the interaction was not significant pair-wise comparisons between the levels of the condition factor were made for each group. Significant differences (Bonferroni correction for multiple comparisons applied) between each pair of conditions of the task were obtained both for the PD group (LS-SA vs. HS-SA: F (1, 19) = 11.18, uncorrected p < 0.004; LS-SA vs. HS-WA: F (1, 19) = 129.63, uncorrected p < 0.001; HS-WA vs. HS-SA: F (1, 19) = 138.58, uncorrected p < 0.001) and the older control group (LS-SA vs. HS-WA: F (1, 19) = 122.04, uncorrected p < 0.001; LS-SA vs. HS-SA: F (1, 19) = 18.55, uncorrected p < 0.001; HS-WA Vs HS-SA: F (1, 19) = 106.80, uncorrected p < 0.001). Thus, for the verb production task and for both subject groups the data show effects of both selection demands and association strength; the condition which requires the longest response time is HS-WA while the fastest condition is that with low selection demands (LS-SA).

In order to investigate whether there were between tasks differences in each subject group we performed two 2x3 repeated measures taskXcondition ANOVAs; the first was carried out for PD patients and the second for older controls. The ANOVA made for PD patients showed significant main effects of both task (F (1, 19) = 8.69, p < 0.01) and condition (F (2, 38) = 115.27, p < 0.001) and also a significant interaction between the two factors (F (2, 38) =

30.87, $p < 0.001$). In view of the interaction post-hoc pair wise contrasts (Bonferroni correction applied) were ran between pair of corresponding conditions of the two tasks. These failed to show differences between the conditions with strong associations (Bonferroni corrections applied; verb-LS-SA vs. noun-LS-SA, (F (1, 19) = 1.92, $p = 0.18$); verb-HS-SA vs. noun-HS-SA, (F (1, 19) = 0.29, $p = 0.59$). However, as far as the HS-WA condition is concerned, PD patients were much slower in producing verbs than nouns (verb-HS-WA vs. noun-HS-WA, F (1, 19) = 59.69, uncorrected $p < 0.001$). A similar 2x3 repeated measures taskXcondition ANOVA was carried out for older subjects. The analysis showed the significant main effect of condition (F (2, 38) = 75.43, $p < 0.001$) and of the two-factor interaction (F (2, 38) = 27.72, $p < 0.001$) but the main effect of task was not significant (F (1, 19) = 0.89, $p = 0.35$). In view of the interaction we run post-hoc pair wise contrasts (Bonferroni correction applied) between pair of corresponding conditions of the two tasks. They showed that older subjects were significantly faster in giving verbs than nouns in the LS-SA condition (Bonferroni corrections applied; verb-LS-SA vs. noun-LS-SA, F (1, 19) = 14.31, uncorrected $p < 0.002$) while showing a trend in the same direction for the HS-SA condition (verb-HS-SA vs. noun-HS-SA, F (1, 19) = 4.96, corrected $p = 0.038$). By contrast, older subjects were slower in producing verbs than nouns in conditions of weak association (verb-HS-WA vs. noun-HS-WA, F (1, 19) = 29.46, uncorrected $p < 0.001$).

In a similar way to what we made for the accuracy data, the main statistical analyses on reaction times were also carried out excluding the correct responses given by the PD patients with latencies between 4 and 6 seconds. Following these analyses the main pattern of results with both verb and noun production tasks still held. Thus the main effect of group found in both noun and verb generation did not depend on PD patients having a longer time in which to respond.

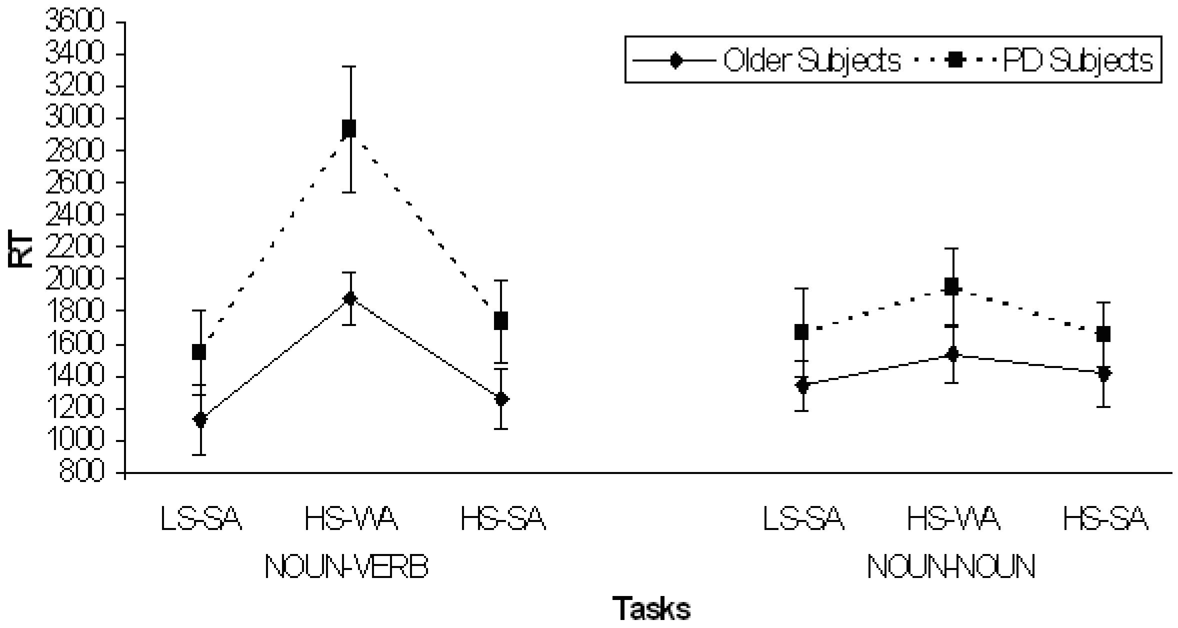

Figure 4.4*:* Response time data for both subject groups in Noun-Verb and Noun-Noun tasks. The conditions of each task are reported in the x-axis while reaction times (RT) are reported in the y-axis expressed in ms. Bars indicate standard deviation. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association.

4.4.3. Older subjects vs. PD patients: Error type analyses

The mean number of errors on the two generative tasks is shown in figure 4.5. For each condition of the two tasks the number of errors made by each PD and older subject was calculated. We then assessed the data for normality. Most of the distributions were not normally distributed; consequently, non-parametric tests were used for the error type analyses. Four types of errors were considered: slow-responses, no-responses, semantic errors and grammatical errors (e.g. a subject gives a noun when required to give a verb). Since semantic errors were very rare in PD patients and virtually absent in older subjects we only included the other three types of errors in the analyses. The error types were considered separately within each task (second graph of figure 4.5) and the analyses focused on the verb generation task given that PD patients performed as well as normal controls in the noun generation task.

Mann Whitney tests executed for the verb generation task (using Bonferroni correction for multiple comparisons) showed that PD patients made significantly more grammatical errors (Mann Whitney U = 98.5, uncorrected $p < 0.01$) and no-response errors (Mann Whitney U = 106, uncorrected $p = 0.01$) than older subjects in this task. Each task was then divided into its three conditions and for each of these the three types of errors were considered separately (third graph of figure 4.5). As far as the verb production task is concerned grammatical errors were made more often by PD patients than older subjects in each condition of the task (Mann Whitney U = 106.5, uncorrected $p < 0.01$ for the LS-SA condition; Mann Whitney U = 107.5, uncorrected $p < 0.01$ for the HS-SA condition; and Mann Whitney U = 110.5, uncorrected $p < 0.015$ for the HS-WA condition). Interestingly no-response errors were made more often by PD patients than older controls only in the HS-SA condition (Mann Whitney U = 102, uncorrected $p < 0.01$) while only trends were present for this kind of error in the other two conditions ($p = 0.052$ for the HS-WA condition, and $p = 0.068$ for the LS-SA condition).

The Wilcoxon Signed Ranks Test was used to examine whether there were within subject differences in the errors made in the verb production task. In this task, PD patients made significantly more grammatical errors than errors classified as either no-response ($p = 0.036$) or slow-responses ($p = 0.024$). This was not the case for older controls ($p = 0.88$ and $p = 0.255$ respectively). Remarkably, in the verb production task, PD subjects made significantly more grammatical errors than no-response errors only in the HS-WA condition ($p = 0.034$), while only trends were present in the two strong association conditions ($p = 0.055$ in LS-SA and $p = 0.072$ in HS-SA). Older subjects made almost the same number of grammatical errors and no-response errors in each condition of the verb production task (HS-WA condition: $p = 0.9$; LS-SA: $p = 0.608$ and HS-SA: $p = 0.157$).

In sum, PD patients most often made grammatical errors in verb production whereas older subjects made this kind of error as often as no-response errors. Furthermore it was in the critical weak association condition that PD patients made grammatical errors more often than no-response errors.

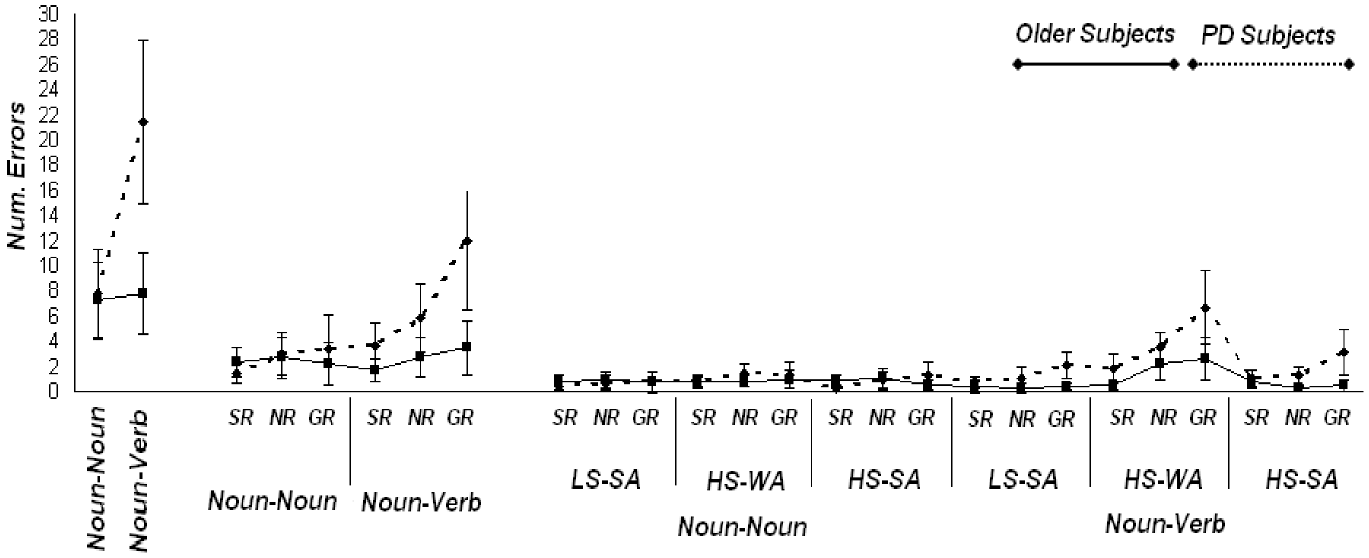

Figure 4.5*:* Error profiles of both subject groups in each condition of the tasks. The mean number of errors for PD and Older subjects in both generative tasks is showed in the graph on the left. The different kind of errors (mean number) made by PD and Older subjects in both tasks are reported in the graph in the middle. The graph on the right shows the different kinds of errors that subjects made in each condition of the two tasks. SR stands for Slow-Response; NR stands for No-Response; GR stands for Grammatical-Error. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Bars indicate standard deviation.

4.4.4. Correlation Between motor and neuropsychological status and performance in PD patients

We investigated whether the impaired performance of PD subjects in the verb generation task and also in the weak association condition of the noun production task could be associated either with their motor impairment measured by UPDRS motor scores or with the neuropsychological tests carried out by the patients. The correlation between UPDRS motor scores and error rate in the verb generation task was not significant either for global performance in the task (Rho = -.379, p = .10) or for errors made only in the HS-WA condition of the task (Rho = -.353, p = .12). The UPDRS motor score was also not correlated with performance on the noun production task, either for global performance in the task (Rho = .007, p = .97) or for errors in the HS-WA condition (Rho = -.074, p = .75). As far as the response time data are concerned, we did not find any significant correlation between the UPDRS scores and RT in either the verb or noun generation tasks (Rho = .288, p = .21; Rho = .088, p = .71 respectively). The correlations were not significant even when only the RT data of the HS-WA condition of the two tasks were considered, (Rho = .21, p = .37; Rho .047, p =

.84 for verb and noun production respectively). UPDRS motor scores were also not correlated with the number of missed responses in both tasks.

As far as the neuropsychological tests are concerned, there were strong correlations between the error rate on the verb production task and the PD patients' scores on a number of tests sensitive to frontal lobe dysfunctions (Rho = -.611, $p < 0.005$ for correlation between the Brixton test score and verb generation performance; Rho = .684, $p < 0.002$, for correlation between the Stroop score and error rate on verb generation; Rho = .544, $p < 0.02$, for correlation between the FAB score and error rate; Rho = -.603, $p < 0.006$ for correlation between the Trail Making Test section B score and error rate). The same correlations also held when the weak association condition of the verb generation task (HS-WA) was considered alone.

Interestingly, no correlations were observed between the same neuropsychological tests and performance on the noun production task, both when it was considered globally (Rho = -.366, $p = 0.11$ for correlation between the Brixton test score and error rate in noun production; Rho = .314, $p = 0.17$, for correlation between the Stroop score and error rate; Rho = .27, $p = 0.24$, for correlation between the FAB score and error rate on noun production) and when it was considered only in its weak association condition. However, there was an exception: PD patients' performance on the noun generation task was correlated with the scores they obtained on the Trail making test section B (Rho = -.534, $p < 0.02$, for global performance on noun production, and Rho = -.519, $p < 0.02$, for errors made only in the HS-WA condition of the task).

4.4.5. Analysis of covariance and correlation between Task Relevant Response (TRR) ratios and performance in PD patients and older subjects: the role of TRR and associative strength in verb production

Correlation between TRR and subjects' performance

We have also investigated whether any correlation exists between the values of TRR and subjects' performance on the two tasks. We found strong correlations between the TRR ratios of stimuli used in the verb generation task and performance on this task; this occurred both in PD patients (Rho = -.636, $p < 0.001$) and in older subjects (Rho = -.523, $p < 0.001$). The higher were the values of TRR the better was the performance. Interestingly we found a correlation between the TRR ratios of stimuli used in the noun generation task and performance on this task in PD patients (Rho = -.246, $p < 0.05$), but not in older controls (Rho

= -.079, p = 0.51). Such a result was probably due to a ceiling effect in the noun generation performance of older controls.

Correlations were also ran between the number of grammatical and no-response errors, made by both PD patients and older subjects in the HS-WA condition of verb generation, and the TRR ratios of the corresponding stimuli. As far as grammatical errors are concerned, a significant correlation between their number and TRR ratios was found, in the HS-WA condition, for PD patients (Rho = -.423, $p < 0.05$) but not for older subjects (Rho = -.064, p = .77). When no-response errors were considered none of the correlations reached significance.

Analysis of covariance

In order to investigate whether TRR ratios or associative strength or possibly both was the key factor as far as the deficits observed in the PD patients in the most problematic condition of verb generation (HS-WA) are concerned, we ran two ANCOVAs (one on verbs and one on nouns), both with the number of errors on each word made by patients in the appropriate group as the dependent measure. In each of the two ANCOVAs the three standard conditions (LS-SA; HS-WA; HS-SA) were contrasted and TRR ratios were used as a covariate. For verbs we excluded all word stimuli with %TRR > 8.8 in order to have the same range of %TRRs for the critical HS-WA condition as for the other two conditions; in a similar fashion, for nouns, we excluded all words with %TRR below 64.4 or above 93.3. Such operations on stimuli led to a range of 13-23 words per condition.

The first ANCOVA was carried out for verbs. This analysis showed an effect of the covariate (TRR), (F (1, 53) = 5.05, $p < 0.03$), that resembles the correlation found between TRR ratios and performance on the verb generation task, and also a highly significant effect of the fixed factor (condition at three levels) (F (2, 53) = 18.51, $p < 0.001$). A series of post-hoc tests were carried out between the levels of the condition factor using Bonferroni corrections for multiple comparisons. These tests showed that the HS-WA condition was significantly different (i.e. worse performance) from the two conditions with strong associations (LS-SA vs. HS-WA, F (1, 34) = 16.67, uncorrected $p < 0.001$; HS-SA vs. HS-WA, F (1, 41) = 33.4, uncorrected $p < 0.001$) while the comparison between the two was not significant (F (1, 30) = 0.42, p = 0.84). The ANCOVA carried out for noun generation did not produce any significant effect, either of the covariate (F (1, 49) = 0.22, p = 0.65) or of the condition factor (F (2, 49) = 2.29, p = 0.11).

To summarize, the results of the ANCOVA made on verbs supports the correlation between TRR ratios and error rates in the verb generation task, and hence confirms that the

TRR is an important factor in explaining the performance of PD patients on this critical task. However, the ANCOVA also suggests that the TRR is not the only factor accounting for the problems shown by PD patients. Associative strength is also important in determining the poor performance that PD patients had in the HS-WA condition of verb generation relative to the other two conditions of the task.

4.4.6. PD patients' medication and single word production

As reported in the text there are differences in medication taken by the patients. Twelve patients were only on dopaminergic medication, while the remaining eight were also taking non-dopamine medications. In particular, three patients were taking MAO-inhibitors, one patient was taking Amantadine, one patient was taking Trasodone, one patient was taking catechol-O-methyltransferase inhibitors, one patient was taking Clozapine+catechol-O-methyltransferase inhibitors, and another one was taking Clozapine+Lorazepam+Sertraline. Of these eight patients only the latter two showed increased difficulties at the neuropsychological assessment performing particularly poorly in: a) both versions of the Story free recall test, b) WCST, c) Trial Making Test Section B (one patient), and in d) Matrices of Raven (one patient). In order to assess the influence on cognition of non-dopamine medications (Moussa, Youdim, & Bakhle, 2006; Meco & Bernardi, 2007) we excluded these two patients from the population of PD patients (n=18) and we run again the main statistical analyses. When two three-factor, 2x2x3, ANOVAs with repeated measures (Group: Patients vs. Older controls; Task: Noun and Verb production; Condition: LS-SA, HS-WA, HS-SA) were carried out, one for accuracy and one for reaction times, the same pattern of results as that obtained for the entire PD population (n=20) held. Thus we may exclude the possibility that the PD patients' difficulties with verbs are crucially influenced by the effects of non-dopamine medication.

4.4.7. Summary of results

PD patients were impaired in the verb production task with respect to normal age-gender-education matched controls, performing significantly worse in all conditions of the task. By contrast, they performed in the normal range in noun production (see figure 4.3).

As far as accuracy performance on the verb generation task is concerned, both groups of subjects were less accurate in situations of weak stimulus-responses association strength (HS-WA) than strong stimulus-response association strength (LS-SA and HS-SA). A significant groupXcondition interaction was obtained for accuracy suggesting that PD patients performed the HS-WA condition extremely poorly. However, it is not possible to rule out the possibility that the significant interaction may derive from a ceiling effect for the older subjects on the accuracy measure in two of the conditions. PD patients, but not older controls, also showed an effect of selection demands (i.e. HS-SA performed worse than LS-SA) in the accuracy data of the verb generation task. When performance on the noun production task is considered an effect of association strength (i.e. HS-WA performed worse than HS-SA and LS-SA) was present in the accuracy data of PD patients but not of older subjects even though there was no overall effect of group. In a similar fashion to the verb generation task, PD patients were significantly less accurate in producing nouns in the HS-WA condition than in the two conditions with strong associations. A significant groupXcondition interaction was in fact obtained for accuracy in the noun production task.

As far as response times are concerned, the results indicated that PD patients were slower than older controls in all conditions of the two tasks. However there were not significant groupXcondition interactions (see figure 4.4). PD patients showed an effect of association strength in both tasks (i.e. HS-WA slower than HS-SA and LS-SA) and also an effect of selection demands (i.e. HS-SA slower than LS-SA) in the verb generation task. Older controls showed effects of association strength and selection demands in the verb generation task but none of these effects were clearly evident in the noun generation task.

The analysis of error types showed that PD patients made more grammatical errors than older controls in each condition of the verb production task whereas differences between subject groups were much less evident in the number of no-response errors (see figure 4.5). PD patients also made more grammatical errors than no-response errors specifically in the weak association condition of the verb production task. By contrast, older controls did not show differences between these two kinds of errors in any condition of the task.

Significant correlations were also obtained between the performance of PD patients in the verb production task and both neuropsychological tests and TRR ratios. The latter were also correlated with PD patients' performance on the noun production task. Finally, the analysis of covariance showed that associative strength is an important factor in determining the extremely poor performance of PD patients in the HS-WA condition of the verb production task.

4.5. General discussion

4.5.1. Interpretation of PD patients' impairments both within and beyond the domain of language

A first interpretation of the global pattern of results found in PD patients might be that they find word generation tasks more difficult than normal controls. However, the evidence of similar levels of accuracy between patients and controls in the noun production task rules out an explanation of global difficulty in generating words in PD patients. An account related to task difficulty for the problems that PD patients have in the verb production task would be that verb generation is more difficult than noun generation. In fact, there is evidence suggesting that verbs are indeed more difficult than nouns. Thus Gentner (1981) has shown that verbs are harder to remember, more slowly acquired by children and are more broadly defined than nouns (she reported that the 20 most frequent verbs have an average of 12.4 word senses each, while the 20 most frequent nouns have an average of 7.3 word senses each). Consistent with this view the analysis based on TRR might be taken to indicate that verb generation is more difficult than noun production. Moreover the evidence that PD patients made more errors in the strong association conditions of the verb generation task relative to the same conditions of the noun generation task might further suggest that verbs are more difficult to generate than nouns. For the noun production task, PD patients made more errors in the weak association condition than in the strong association conditions. The weak association condition of this task was also associated with lower values of TRR relative to the strong association conditions and this indicates that the weak association condition is intrinsically more difficult than the other two conditions.

Another possibility, however, is to consider the impaired performance of PD patients with verbs as due to a specific deficit within the language domain. Generally, studies of language disturbances in PD patients have led to conflicting results so it is not clear whether specific language deficits form part of the PD patients' neuropsychological profile. However, there have been reported studies showing deficits in PD patients when they performed tasks of syntactic judgements (Tweedy, Langer, & McDowell, 1982), when they were required to apply grammatical rules (Ullman et al, 1997), and when they had to learn new verbs (Grossman, Stern, Gollomp, Vernon, & Hurtig, 1994). In the third of these studies the authors reported a verb-learning impairment in PD patients and suggested that the deficit could be accounted in terms of memory deficits in some of the patients while it was likely to be due to some compromised aspects of grammatical processing in most of the patients. Moreover, as reported in the Introduction, Péran et al. (2003) advanced the possibility that the verb generation impairment found in their PD patients could be due to a grammatical deficit. Nevertheless the authors of this latter study did not discuss this deficit further, merely assuming that “the deficit for verb production we observed is related to a grammatical impairment as a consequence of a dysfunction of the frontal cortex in nondemented PD patients” (Péran et al, 2003, p. 155). Indeed there is evidence that nouns and verbs are processed in different brain regions with verbs activating the left prefrontal cortex in particular while nouns activate the left inferior temporal lobe (Shapiro et al., 2006). Nonetheless, there is also evidence against such a distinction between verb and noun processing. For instance, Tyler, Russell, Fadili, and Moss (2001) reported activation of a large semantic network extending from the left inferior frontal cortex into the inferior temporal lobe for both word classes.

As briefly reported in the Introduction of Chapter 2, there have been reports of evidence against the idea of an isolated grammatical deficit in PD patients and more generally against a language specific function of BG (Longworth et al., 2005; see also Katsarou et al., 2003). For instance, Hochstadt, Nakano, Lieberman, and Friedman (2006) found that the errors made by a population of PD patients in a sentence comprehension task correlated with measures of verbal working memory span and cognitive set-switching ability. In a similar way, Grossman et al. (2002) found that the performance of PD patients on various executive functions tests was impaired and correlated with their faulty sentence comprehension. For instance, they found that performance in sentence comprehension was correlated with that on the Trail B test and the Stroop test. These authors suggested that performance on executive tests involving inhibition and planning was related to that on sentence comprehension.

In line with this evidence we have reported an association strength effect in the noun production task for the PD patients and also significant correlations between executive measures (Stroop test, Trail B, Brixton, and FAB) and performance in the verb production task. Thus, our results would support the hypotheses that PD patients’ language impairments are not due to language specific deficits.

4.5.2. The current interpretation

The condition with weak stimulus-response association strength (HS-WA) was the most critical for PD patients. This was the case for verb production and also, to a minor extent, for noun production. As originally suggested by Martin and Cheng (2006) weak stimulus-response associative links require controlled semantic retrieval. According to Badre &

Wagner (2002; see also chapter 1) controlled semantic retrieval comes into play when bottom-up activation of the target representation is insufficient to result in recovery of the relevant knowledge. In comparison to automatic semantic retrieval, controlled semantic retrieval is “1) slower and more effortful; 2) can bias retrieval of task-relevant information even in the face of stronger; prepotent task-irrelevant representation and 3) it can either directly or indirectly inhibit the retrieval of prepotent, task-irrelevant information” (Badre & Wagner, 2002; p. 207). On the contrary, in situations in which strong associations exist between the retrieval cues (noun stimuli in our case) and the relevant knowledge, automatic semantic retrieval should take place. In our experimental paradigm strong stimulus-response associations occur in both situations of high selection (HS-SA) and low selection (LS-SA). Automatic semantic retrieval should be possible in both of these conditions. Badre and Wagner’s theory (2002) can be viewed as a specific instantiation of the operation of the SAS as modulating the operations of the CS as contrast with CS operating alone (Norman & Shallice, 1986). As already shown, in Norman and Shallice’s view, CS concerns the routine selection of actions. In situations of automatic semantic retrieval lemma selection is such a routine operation. On the other hand, a SAS system is required in non-routine tasks to “bias” the activation levels of the units involved in contention scheduling. In Badre and Wagner’s terms (Badre & Wagner, 2002; Badre et al., 2005) this would correspond to controlled semantic retrieval.

However, the contrast between controlled and automatic semantic retrieval does not explain the full pattern of results observed in our PD patients and in particular those obtained in the verb generation task. In fact, we showed that PD patients performed worse than older controls not only in the weak association condition of the verb generation task but also in the two strong association conditions of this task. More importantly PD patients also showed an effect of selection demands on the verb generation task both in accuracy and response times. Indeed, they performed poorer and slower in the HS-SA than in the LS-SA condition. This suggests considering in more detail the cognitive requirements of a task such as verb generation. This is particularly important when the results of the TRR analysis are borne in mind.

4.5.3. Cognitive mechanisms involved in verb production

As previously discussed, 45 normal subjects were asked to provide the first word that came into their mind for each noun stimulus. Each stimulus used in the two tasks was then associated with a measure that we called *Task Relevant Response (TRR;* see figure 4.2). The

TRR ratios gave a measure to what extent each noun stimulus elicited responses that were relevant with the task that had to be executed (either verb or noun production). Moreover the TRR analysis showed that 80% of the responses to the noun stimuli consisted of other nouns, while verbs formed about only 6% of the response set. In other words, in most of the cases a noun was spontaneously associated to another noun. This indicates that, in the verb production task, even when strong associations between nouns and verbs exist, a shift has to be made abandoning the default responses (nouns) in favour of the task relevant ones (verbs).

Recently, Thompson-Schill and Botvinick (2006) have considered verb generation within a Bayesian framework which was based on three main assumptions. First they assumed that a set of response representations is triggered by a stimulus and this set would represent a probability distribution that resembles a pattern of responses that one would obtain in a free association task. Second, they argued that such a probability distribution is translated by a second process into a single response. Third, they claim that the probability distribution over the representations of the responses is also influenced by task representation as well as by the stimulus. The authors suggested that in the case of verb generation, task representation shapes the probability distribution by scaling up the probability of verbs and scaling down that of non-verb responses. In other words, task representation biases the distribution of the responses toward verbs. They argued that the LIFG is the source of such a control process although they refrained from giving a specific localization for the basic framework briefly described above.

In our study the TRR analysis showed that, in the verb generation task, the stimulus nouns of the HS-WA condition were less often associated with the appropriate responses (i.e. verbs represented less than 3% of the responses; see figure 4.2) than were nouns in the other two conditions. The same analysis when carried out for the conditions of the noun generation task showed that, in a similar fashion to the verb production task, the nouns in the HS-WA condition were associated with the highest values of task-irrelevant responses in comparison with the nouns of the strong association conditions (however, in the HS-WA condition of noun generation, the task-irrelevant responses were much less than the task-relevant responses; in fact nouns formed 73% of total responses in this condition; see figure 4.2). Thus, in both tasks a weak association between stimulus and response leads to a higher number of task-irrelevant responses, which in turn indicates increased interference in giving answers which are not strongly associated with stimuli. As already shown, in our study TRR ratios correlated, in both subject groups, with accuracy performance on the verb generation task. However, only for the PD subjects did the TRR values correlate with the number of grammatical errors made in the critical HS-WA condition. In terms of the Thompson-Schill and Botvinick's model, the HS-WA condition would require a high degree of control in order for the probability of verbs to become higher than those of non-verb responses.

As far as PD patients' performance on the two tasks is concerned, we showed that they were much better in giving nouns than verbs in the HS-WA condition. Such a difference was much more marked in the patients than in older controls. Accordingly, we argue that the production of weakly stimulus-related verbs poses more demands for cognitive control than the production of weakly stimulus-related nouns. Verb production occurs in a context in which prepotent, task-irrelevant competitors (i.e. noun responses) are strongly activated; by contrast during noun production task-irrelevant responses (i.e. verb responses) are much less activated. Thus, the poor performance of PD patients in the HS-WA condition of verb generation may be due to their inability to access task-relevant responses in the context of both weak stimulus-responses association strength and highly activated task-irrelevant competitors. In other words, as also suggested by the ANCOVA carried out for verbs, both association strength and ease of selection of task-relevant over task-irrelevant responses (TRR) are important factors in determining the deficit of PD patients in the HS-WA condition of verb generation.

4.5.4. What kind of problems do PD patients have in producing verbs?

Our empirical results suggest that both factors of stimulus-response association strength and selection between competing alternatives are important in determining whether a response can be produced in PD patients. Our interpretation of PD patients' deficits would extend the "two-process model of fronto-temporal control of semantic memory" proposed by Badre et al. (2005), namely the processes of controlled (associative) retrieval and selection during retrieval, by suggesting that BG may have a role in both of the two processes considered in this model. According to our results, when semantic retrieval occurs through bottom-up (automatic) mechanisms, the selection of task-relevant responses is successfully accomplished most of the time but it is poorer and slower in situations of high competition between alternative options (HS-SA) than in situations of low selection (LS-SA). Thus, the process of selection of responses from amongst retrieved task-relevant competitors is a process that is affected in PD patients. On the other hand, with weak associations, retrieval of task-relevant responses requires top-down (controlled) mechanisms (mediated by left anterior VLPFC in the model of Badre et al., 2005) which must specify the general class of an appropriate response (i.e. verbs in the context of many active nouns in the verb generation task). This process also appears to be impaired in PD patients. Often irrelevant information prevails over the relevant one in these patients (i.e. nouns are produced instead of verbs).

The extension to BG structures of the Badre et al.'s (2005) model of control of semantic memory, receives support from evidence which shows that PD patients have problems in both response selection and inhibition of competing alternatives (Longworth et al., 2005; Castner et al., 2007; Castner et al., 2008) and in lexical and semantic retrieval (Crosson et al., 2003; Higginson, Wheelock, Carroll, & Sigvardt, 2005). One possibility is that our PD patients suffer from a dysfunction of the frontostriatal circuit which connects the ventral regions of the caudate to the ventral regions of the frontal lobe, including both regions of the VLPFC considered by Badre et al. (2005) to be crucial in post retrieval selection and in controlled semantic retrieval. However, the functions of the VLPFC have been held to remain relatively intact in mild PD (Owen, 2004), an interpretation which if correct, would point to the importance of the role of the BG for correct performance on the verb generation task in general, and more particularly, on the most critical condition of this task (i.e. HS-WA).

Our results are also in accord with the suggestion of Cools, Barker, Sahakian, and Robbins (2003) who argued that L-Dopa may normalize dopamine levels in many areas of the brain of PD patients (particularly in early PD), such as the dorsal striatum (connected to the dorsolateral prefrontal cortex), while "detrimentally overdosing the relatively intact ventral striatum and its connections to the ventral prefrontal cortex" (Cools et al., 2003, p. 1431). As has recently been proposed (Braver & Cohen, 2000; Cools et al., 2001; 2003; see also chapter 1), dopamine might have a key role in the ability to access task-relevant information because it would facilitate a "focusing" cognitive function by gating task-relevant while inhibiting task-irrelevant corticostriatal projections. Thus our study seems also to confirm the position of Cools et al. (2003) that dopaminergic medication may impair cognitive performance depending on the level of dopamine in underlying cortico-striatal circuits.

4.6. Conclusions

Our results strongly suggest that the key factor which is likely to explain the performance of PD patients in word generation tasks should not be looked for within the grammatical domain per se. The defective generation of verbs of PD patients appears to be due to the default structure of the semantic network in which nouns are most often associated to other nouns. Controlled semantic retrieval and selection between alternative responses (Thompson-Schill et al., 1997; 1998; Badre & Wagner, 2002; Badre et al., 2005; Martin & Cheng, 2006) represent the roles that both the BG and the LIFG (left anterior and mid VLPFC according to Badre et al., 2005; see also Robinson et al., 1998; 2005; see also chapter 2) fulfill in order to both select responses in situation of high competition and responses that appear to be both weakly related with the stimuli and subject to intrusion from irrelevant competitors.

Chapter 5

5.1. Empirical background and aim of the computational model

The findings of the noun and verb generation experiment, carried out on both PD patients and older controls, have shown that both factors of response selection and associative strength influence single word production with the latter having a greater impact on performance than the former. Indeed both subject groups performed the weak association condition of the verb generation task worse (lower accuracy and slower RT) than the strong association conditions. A similar patter of performance was also shown by PD patients on the noun generation task. On the other hand, an effect of selection demands (HS-SA performed poorer than LS-SA) was only evident in the verb generation task, and in this task it occurred in the RT data of both subject groups but in the accuracy data of only PD patients. Importantly, our findings also suggested that task-irrelevant responses differently affect the performance in the two tasks. In particular noun responses interfere during verb generation more than verb responses do during noun generation. More specifically, the findings indicate that noun responses interfere particularly during the production of weakly stimulus-related verb responses, namely during the condition of verb generation with weak stimulus-response associative strength (i.e. HS-WA). Thus, in a similar fashion to Badre et al., (2005) and also to Thompson-Schill and Botvinick (2006) we have shown that when associative strength is manipulated across task conditions this can also result in variable competition because of the presence of irrelevant competitors predominantly in situations of weak stimulus-response associative strength.

In the domain of verb generation the competitive versus association strength debate (Thompson-Schill et al., 1997; 1998; Martin & Cheng, 2006, respectively) (see chapter 4) has led to the proposal of two different demonstrative models (i.e. not fitted to any experimental data). Thompson-Schill and Botvinick (2006) have proposed a model to reconcile selection and association strength in a Bayesian “competition model”. This model relied on the strength of cue-response associations (e.g., apple-eat) as well as on inhibitory connections between competing responses (e.g., eat vs. harvest) (see figure 5.1). In more detail their model rested on three assumptions. First, the presence of a stimulus triggers a pattern of activation across a set of potential response nodes. This pattern of activation would be similar to that obtained using free association norms. Second, they assume that a second process translates the probability distribution into a single response; the latency of a response is assumed to vary inversely with its probability value. Finally they also assume that the task representation may shape the probability distribution over the candidate responses. Thus in the case of verb generation, the task representation would bias the distribution of the responses toward verbs, increasing their probability and decreasing that of nouns.

Thompson-Schill and Botvinick have also tried to take into account the finding of Martin and Cheng (2006) of equal RT on the conditions with strong association of their task (i.e. HS-SA and LS-SA in our paradigm). The authors report the results of preliminary simulations obtained using a simple two-layer network model of response selection in which a stimulus node was connected to two response nodes which in turn were connected with each other by reciprocal inhibitory links (Usher & McClelland, 2001; see figure 5.1). The weight of the connections between the stimulus and the two response nodes could be either equally distributed between the two links (i.e. 0.5 and 0.5) for the condition with high selection demands and strong association (HS-SA), or unbalanced between the links (i.e. 0.9 and 0.1) for the LS-SA condition. The authors showed that the speed with which a response node was chosen depended on the degree of competition between the response nodes (Verb1 and Verb2 in the figure); thus there were values for the parameter controlling the strength of the reciprocal inhibitory connection weights between the two response nodes (i.e. parameter ß in their model), under which the two conditions yielded nearly identical RT.

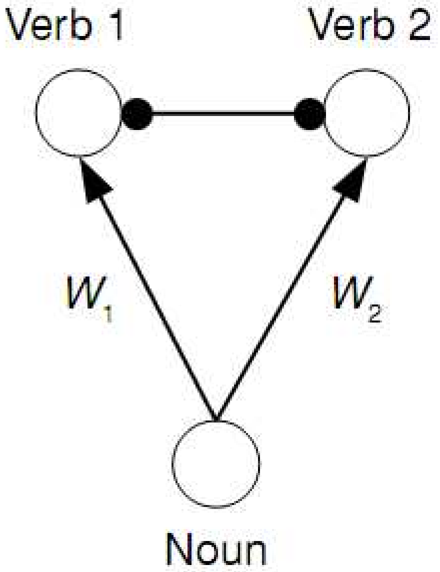

Figure 5.1. Application of the Usher and McClelland’s model (2001) to verb generation by Thompson-Schill and Botvinick (2006). W_1 and W_2 represent connection weights between the noun stimulus and the verb responses. Inhibitory connection weights between the verb units are controlled by parameter ß (not shown).

As far as the weak association condition of the Martin and Cheng's (2006) paradigm is concerned, Thompson-Schill and Botvinick (2006) claim that this condition is also of higher selection demands than the conditions with strong association given that competition from non-verb responses would be particularly high in situations of weak association. Thus, differently from Martin and Cheng (2006) and Martin and Byrne (2006), but also from Thompson-Schill et al., (1997; 1998), Thompson-Schill and Botvinick (2006) acknowledge that non-verb responses may have a role in verb generation.

In response to Thompson-Schill and Botvinick (2006), Martin and Byrne (2006) have proposed a model of verb generation that did not involve any true competitive mechanism (i.e. direct inhibition between response nodes). Their model rested on the spread of activation across associative connections between cue and responses. In a similar way to Thompson-Schill and Botvinick, Martin and Byrne also assume that task representation has an important role for the retrieval of verb responses. In particular they claim that it leads to the activation of the concept "action" during verb generation (see figure 5.2). The selection of a response in this model would be determined by the conjoint activation from the noun cue and from the "action" concept. The strength of the associative links between the noun cue and its associated responses and between the concept "action" and the verb responses (these latter associative links are assumed to be of equal strength in Martin and Byrne's model) influence the strength of the spread of activation in the associative semantic network of Martin and Byrne. According to these authors, the associative strength between the noun cue and the most frequently produced verb is directly reflected in the RT to produce the verb, irrespective of the strength of competing responses. In other words, they claimed that the simple relation between associative strength and latency of verb response production accounts for the data of their experiment (i.e. Martin & Cheng, 2006).

However, Martin and Byrne have proposed that a different mechanism is also involved in situations of weak stimulus-response associative strength (HS-WA), namely one of controlled search of memory. This mechanism operates when the activation of no response nodes overcomes the threshold within a certain amount of time. Briefly, they speculate that in this type of situation the activation of the concept "action" is strategically varied (i.e. increased and decreased) and that this concept is used together with the non-verb associates, which spontaneously spring to mind, to find a verb related to the initial noun cue. Martin and Byrne propose that such a mechanism could in principle explain the performance of their subjects in the condition with weak association (i.e. longer RT relative to the conditions with strong association).

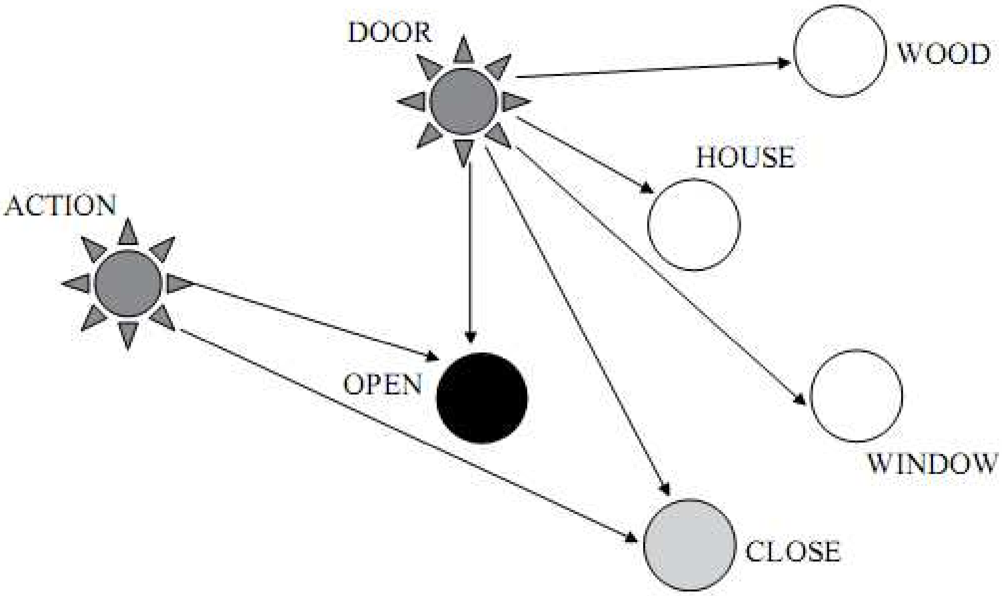

Figure 5.2. The noncompetitive model of Martin and Byrne (2006). The figure illustrates spreading activation from both the concept associated with the noun stimulus *door* and from an “action” concept. In the figure the darkness of the associated concept nodes indicates the degree of activation.

In sum, both models briefly sketched above offer interesting accounts for subjects’ behavior on the verb generation task; however none of these models implement its assumptions in a detailed way so that it is not clear how executive control mechanisms interact with associative retrieval to produce the observed verb generation performance. For instance, Martin and Byrne pointed out that the preliminary simulation of Thompson-Schill and Botvinick failed to address the role of non-verb competitors. They also raised the question of which kind of model, if any exists at all, whould be required to accommodate different sets of results (i.e. both the effects of selection demands and association strength). Finally, Martin and Byrne also claimed that without any further computational evidence their own model should be preferred to that of Thompson-Schill and Botvinick given that it explains, in principle, the same data without referring to any competitive mechanism.

In this chapter we present our proposal of a model of verb generation which rests on the functional interaction between executive control and associative retrieval. Our model also extends to noun generation and tries to explain and reproduce the performance that older controls, PD patients, and young adults show on both these tasks. Indeed, we have also obtained a standard of performance on single word generation tasks by administering young adults the same noun and verb generation tasks. In the first part of this chapter we present the results of this experiment.

Our cognitive model relies on basic models of associative retrieval (ACT-R memory theory; Anderson et al., 2004) and on simple mechanisms of executive control (Nigg, 2000; Stuss et al., 2005). According to our proposal verb and noun generation consists of three processing stages: (1) allocation of attention on retrieval cues, (2) associative retrieval, (3) and response inhibition. Moreover we also assumed that the release from a retrieval failure and the initiation of a new retrieval attempt require time and executive resources. The model was tested in a simulation which was aimed to reproduce the performance of young adults, older adults, and PD patients on noun and verb generation. The results of the simulation show that PD patients and older controls differ particularly in the ability to inhibit task-irrelevant responses and in the speed of release from a retrieval failure.

More generally, our model shows that both the accounts of verb generation of strength of association and inhibition/competition can be integrated into one coherent model by assuming that they apply to two distinct stages. Thus they need not be considered as alternative accounts as was originally argued (Thompson-Schill et al., 1997; 1998 vs. Martin & Cheng, 2006) or alternative viewpoints on the same thing as it has been recently advanced (Thompson-Schill & Botvinick, 2006 vs. Martin & Byrne, 2006).

5.2. Noun and verb generation in young adult subjects

We carried out an experiment of noun and verb generation in young adults using the same paradigm as that used on populations of older subjects and PD patients. The aim of the experiment was twofold; first, we wanted to appraise the generalizability of the results that we obtained on PD and older subjects and to show that the conclusions reached so far on the relative role of association strength and response competition do not depend on age-related impairments or compensatory cognitive strategies; second, this experiment allowed us to determine a standard of performance for noun and verb generation, which was necessary for the development of a unitary account.

In the experiment, we adopted the same stimuli and methods used on older controls and PD patients. Following our previous results (see chapter 4) we expected to observe a strong effect of stimulus-response associative strength on both tasks. However, effects of selection demands were expected to be less evident since, in our previous study (see chapter 4), they were obtained only in verb generation and they were generally less marked than the effects of association strength; moreover Martin and Cheng reported no RT difference between high and low selection demands conditions (with matched association strength) in a normal adult subject population. Finally, based on both the analysis of Task-Relevant Response (TRR) (see figure 4.2 of chapter 4) and on the results showing that both PD patients and older controls found the HS-WA verb condition particularly difficult, we hypothesized that young subjects could be slower with verbs than nouns in this critical condition. Given the greater efficiency of executive processes in younger participants relative to older subjects and PD patients, we expected to observe the effects mainly on RT. In fact, even though younger participants are usually able to retrieve task-relevant responses also in the face of prepotent task-irrelevant information, the potential inhibition of task-irrelevant responses and the consequent further retrieval attempts require additional time.

Summarizing, in line with our previous results and with the findings of Martin and Cheng (2006) our predictions are that RT is higher in conditions of weak association (vs. strong association) for both tasks (H1; association strength effect), either equal or slightly higher in the high selection-strong association condition (HS-SA) relative to the low selection-strong association condition (LS-SA) (H2; selection demands effect), and more specifically, higher in verb generation (vs. noun generation) in the condition with weak association (HS-WA) (H3; potential interference of non-verb responses).

5.2.1 Methods

Design and Stimuli

Following Martin and Cheng (2006) and our previous experiment (see Chapter 4) the generation of nouns and verbs was examined using noun stimuli belonging to three experimental conditions. In two experimental conditions, the stimuli were matched for stimulus-response associative strength but differed in selection demands (low selection-strong association, LS-SA; high selection-strong association, HS-SA). In the third experimental condition, we used stimuli with high selection demands and weak stimulus-response associative strength (HS-WA). Thus, the design for the verb/noun generation experiment was a 2 (verb generation, noun generation) X 3 (LS-SA; HS-WA; HS-SA) dependent measures design.

As already shown, after two pilot tests twenty-three nouns were selected as stimuli for each of the three conditions of the two tasks; for each noun stimulus we have used the ratio of the response frequencies of the two most common responses as a measure of selection demands (following Thompson-Schill et al., 1997; 1998) and the ratio of the mean association strength of the first two most common responses to the number of subjects who judged noun-verb (and noun-noun) stimuli as a measure of stimulus-response association strength. As proposed by Martin and Cheng (2006; see also chapter 4), the response frequency of a verb (or a noun) was used as an index of its association strength with the stimulus noun. The stimuli used in the noun and verb generation tasks were matched for associative strength (of corresponding conditions), selection demands (of corresponding conditions), frequency, and concreteness (see table 4.3 of chapter 4).

Participants and Procedure

Twenty young adults (10 M and 10 F, age range: 21-27) underwent the verb and noun generation tasks, with the order of administration of the two tasks counterbalanced within the sample and a random presentation of noun stimuli of the three conditions. Participants were asked to produce a verb (or a noun) related to each noun stimulus as quickly as possible within the time limit of 4 seconds. The main dependent variables were RT (msec) and proportion of correct responses.

5.2.2 Results

The results of the noun and verb generation tasks are shown in Figure 5.3. Log-transformed RT and arcsine-transformed accuracy did not violate assumptions of normality (Shapiro-Wilks test).

Accuracy analyses

A 2 x 3 repeated measures ANOVA with task (noun and verb generation) and condition (LS-SA; HS-WA; HS-SA) as within-subject factors was carried out on the proportion of correct responses. The analysis showed the main effect of condition ($F (2, 38) = 4.54, p < .02$) and a significant taskXcondition interaction ($F (2, 38) = 4.50, p < .02$) but the main effect of the task was not significant ($F (1, 19) = 0.91, p = .35$). In view of the significant interaction two repeated measure ANOVAs were carried out, one for each task. These analyses showed a significant main effect of condition for verb generation ($F (2, 38) = 5.62, p < 0.01$) but not for noun generation ($F (2, 38) = 1.05, p = 0.35$). Accordingly, post-hoc pair-wise contrasts were only executed for the verb generation task (using Bonferroni corrections). The tests showed a significant difference between HS-SA vs. HS-WA ($F (1, 19) = 8.11$, uncorrected $p = 0.01$), a trend of LS-SA performed better than HS-WA ($F (1, 19) = 5.26$, corrected $p = 0.033$), and no difference between LS-SA vs. HS-SA ($F (1, 19) = 0.13, p = 0.72$). Thus, the results indicate a marginal effect of association strength for accuracy in verb generation.

In view of the taskXcondition interaction, we also performed post-hoc pair-wise contrasts (Bonferroni correction applied) between pairs of corresponding conditions of the two tasks. As far as the two strong association conditions are concerned, these tests showed that young adults are equally accurate in producing nouns and verbs (verb-LS-SA vs. noun-LS-SA: F (1, 19) = 1.08, p = 0.31; verb-HS-SA vs. noun-HS-SA: F (1, 19) = 0.31, p = 0.58). However a trend for the HS-WA condition was obtained which indicated worse performance with verbs than nouns (verb-HS-WA vs. noun-HS-WA: F (1, 19) = 6.36, corrected p = 0.021).

Reaction time analyses

A 2 x 3 repeated measures ANOVA with task (noun and verb generation) and condition (LS-SA; HS-WA; HS-SA) as within-subject factors was carried out on RT. The analysis showed the main effect of condition (F (2, 38) = 79.22, p < .001) and a significant taskXcondition interaction (F (2, 38) = 23.01, p < .001), but the main effect of the task was not significant (F (1, 19) = 0.89, p = .35). In view of the significant interaction two repeated measure ANOVAs were carried out, one for each task. These analyses gave a significant main effect of condition both for noun generation (F (2, 38) = 14.44, p < 0.001) and for verb generation (F (2, 38) = 86.61, p < 0.001). Post-hoc pair-wise contrasts executed for the noun generation task showed significant differences (using Bonferroni corrections) between LS-SA vs. HS-WA (F (1, 19) = 15.41, uncorrected p < 0.001) and HS-SA vs. HS-WA (F (1, 19) = 26.67, uncorrected p < 0.001) but no difference between LS-SA vs. HS-SA (F (1, 19) = 0.003, p = 0.95). The data show a clear effect of association strength but not of selection demands for RT in noun generation. Post-hoc pair-wise contrasts executed for the verb generation task showed an analogous pattern of results: significant differences (using Bonferroni corrections) for comparisons between LS-SA vs. HS-WA (F (1, 19) = 94.64, uncorrected p < 0.001) and HS-SA vs. HS-WA (F (1, 19) = 108.28, uncorrected p < 0.001), but no difference between LS-SA vs. HS-SA (F (1, 19) = 1.27, p = 0.27). An effect of association strength but not of selection demands was also present in the verb generation task.

In view of the interaction and of our hypotheses we also performed post-hoc pair-wise contrasts (Bonferroni correction applied) between pairs of corresponding conditions of the two tasks. These contrasts showed that young adults were faster in producing verbs than nouns in the condition with low selection and strong association (verb-LS-SA vs. noun-LS-SA, F (1, 19) = 9.75, uncorrected p < 0.007) while showing a trend in the same direction in the other condition with strong association (verb-HS-SA vs. noun-HS-SA, F (1, 19) = 5.17, corrected p = 0.035). Young adults were instead slower with verbs than nouns in the condition with weak association (verb-HS-WA vs. noun-HS-WA, F (1, 19) = 10.37, uncorrected p < 0.006).

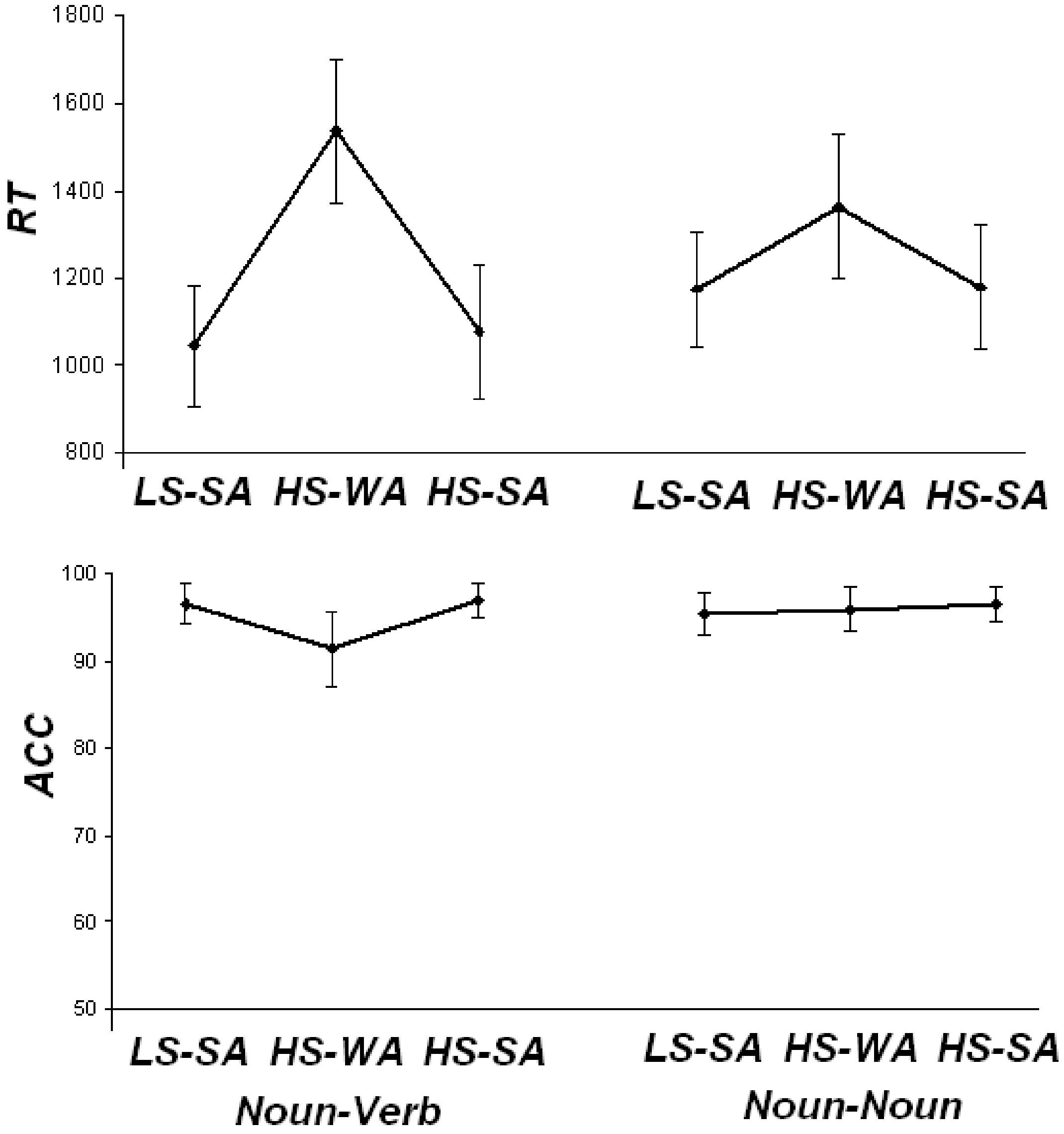

Figure 5.3. Experimental results for young participants in verb and noun generation tasks, plotted by experimental conditions. The graphs at the top of the figure illustrate response time (RT) performance expressed in msec (verb generation is reported on the left). The graphs at the bottom of the figure illustrate accuracy (ACC) performance expressed as percentage of correct responses (verb generation on the left). Noun-Verb and Noun-Noun refer to verb and noun generation respectively. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Error bars indicate 95% confidence intervals.

5.2.3 Discussion

The results show that stimulus-response associative strength has a significant influence on RT in noun and verb generation, and a smaller influence on accuracy in verb generation (thus supporting H1). These results extend existing findings (e.g. Martin & Cheng, 2006; see chapter 4) to a younger age group. H2 was not supported since we did not find any effect of selection demands. In fact, the HS-SA condition was performed equally fast and at similar levels of accuracy than the LS-SA condition in both tasks. The present findings are, however, in line with those of Martin and Cheng (2006) who also did not find any selection demands effects in their young adult sample. Interestingly, a trend for an effect of aging appeared in their study with regard to selection demands. Indeed, their older controls were 350 msec slower in the HS-SA condition than in the LS-SA one (however $p = .22$). As reported in chapter 4, our sample of older controls showed an effect of selection demands on RT in the verb generation task. Nevertheless, as far as selection between alternative responses is concerned and limited to a young adult sample, we can conclude that this factor appears not to play a role in noun/verb generation. This is clearly the case when strong stimulus-response associative links exist in both conditions of high and low selection demands.

The results of the experiment also showed that young subjects performed worse with verbs than nouns only in the weak association condition. By contrast they were somewhat faster with verbs than nouns in the two strong association conditions. The fact that young adults were actually slower with verbs than nouns only in the weak association condition may indicate that this condition of verb generation is particularly prone to interference from task-irrelevant (non-verb) competitors (see chapter 4 for related arguments). Nevertheless the very few errors made by adult subjects in the two tasks and more specifically in the HS-WA condition of verb generation, were mainly represented by missing responses (cf. Chapter 4, no-response errors) rather than by grammatical errors (cf. Chapter 4, i.e. a noun is given when a verb is required). In this respect young subjects behaved in a similar way to older controls and differently from PD patients who made many grammatical errors in the verb generation task.

In the following sections we describe the model that we developed in order to accommodate and explain the findings obtained in our three subject populations. A possible explanation for why the generation of verbs may be easier than that of nouns in the strong association conditions is also advanced.

5.3. The Focus-Retrieve-Inhibit (FRI) model

We propose a novel account of noun/verb generation performance, based on the functional interaction between associative retrieval and executive control operations. This account aims to represent a unitary explanation for the main experimental findings obtained so far and to contribute to the resolution of the competition vs. association strength debate on verb generation. A further important aim of the model is to account for the PD patients' deficits in verb generation.

According to our explanation, noun/verb generation requires three processing stages: (1) allocation of attention on retrieval cues (*F*ocusing) (stage 1, *W,* in figure 5.4), (2) associative retrieval (*R*etrieve) (stage 2, figure 5.4), (3) response inhibition (*I*nhibit) (stage 3, *IP*, in figure 5.4). The first stage requires executive control and involves similar mechanisms to those implied by the first (primary cue, figure 5.4) and third assumption of Thompson-Schill and Botvinick and by the concept of "action" of Martin and Byrne (secondary cue: "noun" and "verb", figure 5.4). The second stage is handled by automatic associative processes and it is assumed by both demonstrative models (i.e. automatic spread of activation in Martin and Byrne and second assumption of Thompson-Schill and Botvinick). The third stage also requires executive control and deals with task-irrelevant competitors. Finally, we also assume that recovering from a retrieval failure and initiating a new retrieval attempt require time and executive resources (i.e. *E* -energization- in figure 5.4; see Stuss et al., 2005). As was shown in the Introduction of the thesis, energization is the process by which the neural system activates the responses for a task allowing prompt response selection and initiation (see Stuss et al., 2005).

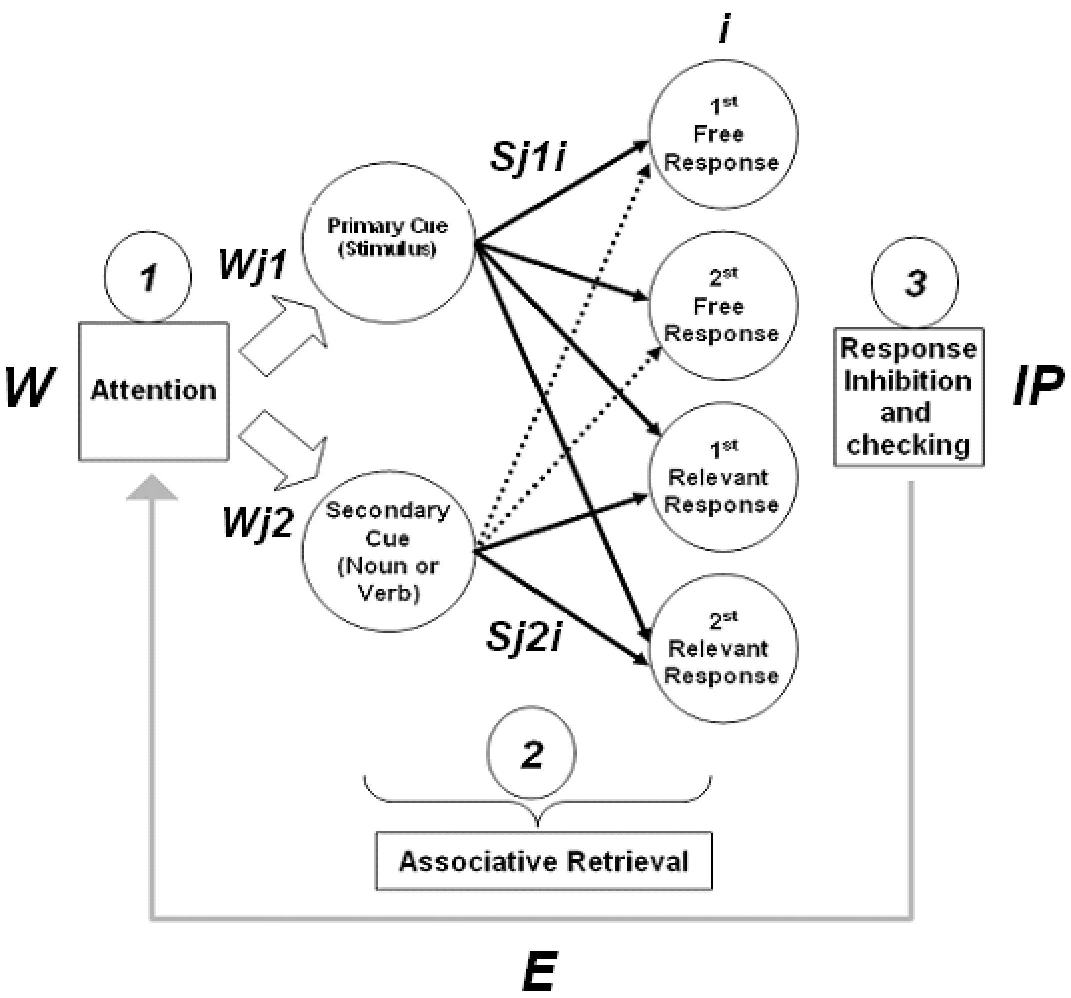

Figure 5.4: Main components and processing steps of the Focus-Retrieve-Inhibit model. The topology of the network structure used in the simulation is also sketched. Primary Cue refers to the noun stimuli used in the experiment. Secondary Cue refers to the "noun" and "verb" concepts (see text for details). Dotted lines represent possible links, whose existence depends on the responses given to the specific noun stimulus in the free association test (1st and 2nd Free Response in the figure) (e.g. such links are more likely to exist for the "noun" secondary cue than for the "verb" secondary cue given that free responses are most often represented by nouns). 1st and 2nd Relevant Response indicate the first and second actual response given by subjects, in the two pilot tests (see Chapter 4), to each noun stimulus of the three experimental conditions of the two tasks. The numbers 1-2-3 refer to successive stages of processing in the model. W is an ACT-R parameter that refers to attention (see text for details); E stands for energization; IP stands for inhibition probability. *Wj1* and *Wj2* refer to the amount of attention focused on the two retrieval cues; *Sj1i* and *Sj2i* refer to associative strength for the links connecting the two retrieval cues with the response nodes *i* (see section 5.3.1 for details on these parameters).

Generally speaking, our proposal is rooted in a Bayesian framework and constitutes a psychologically-plausible implementation of Thompson-Schill and Botvinick's general framework (2006), along the more detailed lines suggested by Martin and Byrne (2006; see also Danker, Gunn & Anderson, 2008). In a similar way to both these models, our account relies on the strength of stimulus-response associations; however, following Martin and Byrne (2006) our model does not rest on a true competitive mechanism, that is, there are not inhibitory connections between competing task-relevant responses (e.g. verb responses) in our model (i.e. note the absence of links connecting *i* response nodes in figure 5.4). Instead, in a similar way to Martin and Byrne (see also Danker et al., in 2008) competition between associate responses is only implemented via the effect of competitors on associative strength in our model (see next section). Thus, in the FRI model the selection of a response is determined by the conjoint activation from the noun cue and from the "verb" (or "noun") concept. In other words, the associative strength between the noun cue and the response nodes (*Sj1i* in figure 5.4; see next section) and between the concept "verb" (or "noun") and the verb responses (or noun responses) (*Sj2i* in figure 5.4; see next section) influence the strength of the spread of activation in our associative network. As in the three-assumption proposal of Thompson-Schill and Botvinick (2006), in FRI a stimulus noun (primary cue; see figure 5.4) triggers a spread of activation across a set of potential responses (free association responses and task-relevant responses, see figure 5.4). Second, simple mechanisms of associative retrieval (see next section) translate the probability distribution of the initial candidate responses into a single response. Third, in our model like in those of Thompson-Schill and Botvinick (2006) and Martin and Byrne (2006), the representation of the task (either noun or verb generation) shapes the probability distribution over the candidate responses.

With regard to the third assumption, we followed Martin and Byrne (2006) in proposing that a simple form of strategic control of retrieval can be based on the dynamic allocation of attentional resources to the "verb/noun" secondary cue (i.e. concept "action" in Martin & Byrne's model) vs. the primary cue represented by the stimulus noun (see Wj1 and Wj2 in figure 5.4). Thus in the FRI model we have concepts of "verb" and "noun" that are used to represent the two tasks (secondary cues; see figure 5.4). In our model the two retrieval cues are initially provided with similar attentional resources (i.e. similar values for Wj1 and Wj2 in stage 1 of figure 5.4; see next section). However we assume that, if retrieval fails (i.e. no task-relevant response is automatically retrieved), more attention is placed on the secondary cue, at the expenses of the primary cue. This attentional modulation is functionally motivated by the need to overcome the most frequent cause of retrieval failure (that we assume to be represented by intrusion of task-irrelevant responses). In fact, giving more attention to the secondary cue increases the probability of success of the next retrieval attempt (see next section), because it binds more tightly the retrieval processes to the desired kind of response (although this may require more effort and be slower than a less constrained retrieval process). Our proposal of attentional modulation of control is similar to the idea of Thompson-Schill and Botvinick (2006) of having a mechanism which, in the verb generation task, operates to bias the retrieval process toward verbs increasing their probabilities and decreasing those of nouns.

As already mentioned in the Introduction of this chapter and at the beginning of this section, unlike from both Martin and Byrne and Thompson-Schill and Botvinick’s models, we explicitly address the issue of how task-irrelevant responses interfere during the generation of task-relevant information and more specifically the potential role of non-verb competitors in verb generation (stage 3, *IP*, of figure 5.4). As already shown, Martin and Byrne have claimed that non-verb competitors do not play an important role in verb generation; by contrast, our findings on PD patients suggest, as also argued by Thompson-Schill and Botvinick, that one has to focus on verb associates in order to exclude non-verb competitors, which will spontaneously spring to mind during verb generation. Following the demonstrative model of Thompson-Schill and Botvinick, who have proposed that response override is sometime required during verb generation (i.e. a strong non-verb response needs to be overridden in favour of a weaker, but task-relevant, response; see Levy & Anderson, 2002; Botvinick, Braver, Barch, Carter, & Cohen, 2001), the FRI model contained a simple mechanism for dealing with such a situation (see section 5.3.4).

As shown at the beginning of this section, the FRI model involves another executive process, namely that of energizing responses (i.e. *E* in figure 5.4). Energization allows subjects to concentrate on a particular task. It is the process whereby the arousal’s energy is allocated to the neural systems in order to promptly initiate the response for a task. As suggested by Alexander (2006), reduced levels of energization may reflect in delayed initiation and pauses at shift points. When shifts occur, for instance between the different demands of a task, the entire recruitment, activation and setting of responses take place again (Stuss et al., 2005; Alexander, 2006). In the FRI model we have assumed that the release from a retrieval failure requires time and executive resources, and that reduced levels of energization may result in delayed initiation of the next retrieval attempt. To give an example, we can consider the case of a retrieval failure in the verb generation task; in such a situation the release from this failure and the subsequent re-allocation of attention must occur in order to face task demands.

5.3.1 Associative retrieval

Our view of associative retrieval is based on the adaptive control of thought-rational (ACT-R) declarative memory theory, which proved able to explain a wide array of experimental findings in memory research (e.g. Anderson, Bothell, Lebiere & Matessa, 1998; Anderson et al., 2004; Danker et al., 2008). Broadly speaking, ACT-R contains a retrieval module that maintains control during the process of retrieval of semantic and episodic information. In ACT-R, such a module is assumed to be located in the left prefrontal cortex (Anderson et al., 2004). The amount of time the control is exerted by this module is determined by the accessibility of the memory as calculated by its activation value. The latter is given by the sum of the base-level activation of the memory (i.e. the amount of previous experience with that memory) and the spreading activation from the cues (i.e. the context). ACT-R implements a Bayesian theory of declarative memory in which the speed and success with which a fact is retrieved from memory is determined by the usefulness and relevance of such a fact and is affected by factors such as recency, frequency, and context. In other words, those memories that are most likely to be needed in the current context are also the easiest to retrieve in ACT-R.

As shown in Figure 5.4 (step 1), associative retrieval is initiated by focusing attention on two cues: the noun stimulus (primary cue) and the secondary cue (“noun” or “verb” node). Activation flows in the network and reaches potential response nodes (see step 2 of figure 5.4). Following ACT-R theory, the final activation of a response node depends on its inherent strength, or base-rate activation, on the strength of its associative links with cues in the current context, and on the attention initially placed on retrieval cues. The two last factors give a measure of spreading activation in the network for a potential response node (Danker et al., 2008). According to ACT-R, the activation (*Ai*) of a response node *i* is thus given by the following activation equation:

$$A_i = B_i + \sum_j W_j S_{Ji} \tag{1}$$

where *Bi* is the base-rate activation of the node, *Wj* is the attentional weighting (fixed initially at the value of 1.0 in ACT-R) placed on the two activation sources in our model (primary and secondary retrieval cues *j*, *Wj1* and *Wj2* in figure 5.4), and *Sji* is the associative strength for the links connecting the retrieval cues with the response node *i* (*Sj1i* and *Sj2i* in figure 5.4). According to ACT-R theory, base-rate activation depends on how recently and frequently a given word node *i* has been accessed in the past (see Danker et al., 2008, for the specific equation).

As far as the spreading activation component of the activation equation is concerned (i.e. *Wj* and *Sji*), we have followed the ACT-R theory in assuming that in the FRI model a similar attentional weight is initially provided to the primary and the secondary cues. In other words, the two sources of activation in our model, *Wj1* and *Wj2,* are initially assigned similar values (i.e. approximately 0.5 each). On the other hand *Sji* gives the probability with which a certain retrieval cue *j* predicts the fact *i*. As far as the secondary cues are concerned, in a similar fashion to Martin and Byrne (2006), we have assumed that the links between a given secondary cue node (e.g. “verb” node) and its associated response nodes (e.g. verb response nodes) are of equal strength. In other words, we have one value for the links connecting the secondary cue “noun” with its associated noun response nodes and another value for the links connecting the secondary cue “verb” to its associated verb response nodes (both these kinds of links are indicated by *Sj2i* in figure 5.4). We have used the ACT-R’s associative strength equation (2) in order calculate the probability with which each secondary cue predicts its associated facts.

$$Sj2i = S - ln(fanj2) \tag{2}$$

where *Sj2i* takes two values, one for the secondary cue “noun” and one for the secondary cue “verb”. *S* is a parameter which expresses the maximum associative strength and *fanj2* is the number of associations of cue *j2*. In ACT-R, associative strength is generally spread equally among each of the associate nodes such that, as the number of associates increases the spreading activation to each node decreases. Thus, the extent to which a cue can predict a fact decreases as the number of associated facts increases (Sohn, Goode, Stenger, Carter, & Anderson, 2003; 2005; Danker et al., 2008). As mentioned above (see also appendix 2), we have used this equation to calculate the associative strength between each secondary cue (i.e. “noun” and “verb”) and all its associated facts (i.e. all noun response nodes for the concept “noun”). Because in the language, and in our sample of responses (i.e. see free association norms reported in chapter 4), nouns are more numerous than verbs (i.e. there is a higher *fanj2* in equation 2 for the “noun” secondary cue than for the “verb” secondary cue), the associative strength between the concept “noun” and all its related facts is lower than the associative strength between the concept “verb” and all its associated facts. In other words, *Sj2i* is lower when the secondary cue is “noun” than when it is “verb” (see appendix 2).

Nevertheless, as suggested by Martin and Byrne (2006), the associative links between the primary cue nodes (i.e. noun stimulus) and their associated response nodes (both task-relevant and free-association response nodes, *Sj1i* in figure 5.4) are not of equal strength. In a similar fashion to our previous study on PD patients (see chapter 4) we used the response frequency of a response as an index of its association strength with the stimulus noun (cf. Martin & Cheng, 2006). Thus, in order to calculate *Sj1i* for each response node *i* (either task-relevant or free-association) we used the ratio of the frequency of the response (which was obtained using the pilot tests described in chapter 4; see also appendix 2) to the number of subjects who judged noun-noun, noun-verb, or noun-free association stimuli (see equation 3 below).

$$Sj1i = f(i)/n \tag{3}$$

where *f(i)* is the frequency of the response node *i* and *n* is the number of subjects who judged the current stimulus noun (primary cue in figure 5.4).

Another important aspect of the declarative memory system of ACT-R concerns the probability of generating a particular response node *i*. This probability is a function of the final activation of node *i* and of the activation of other potential responses. More specifically, the probability of generating a word response node *i* is given by the ACT-R’s equation below:

$$P_i = \frac{e^{\frac{A_i}{s}}}{\sum_j e^{\frac{A_j}{s}}} \tag{4}$$

where *Ai* is the *i* node activation, *j* are all potential response nodes, and *s* is a parameter representing the degree of noise in the memory system. This equation produces a mechanism of response selection similar to that assumed by Thompson-Schill and Botvinick. In fact, these authors propose that the probability to select a response should vary monotonically with its posterior probability which is estimated within the initial probability distribution (i.e. the one elicited by the stimulus). Finally, in ACT-R the time *Ti* that is needed in order to retrieve a particular response node *i* is only related to the final activation of *i* according to the retrieval time equation (equation 5 below):

$$T_i = Fe^{-A_i} \tag{5}$$

where *Ai* is the activation of the node *i*, and *F* is a latency scaling parameter.

The FRI model uses all these equations in order to simulate experimental data.

5.4. Cognitive simulation

5.4.1 Methods and rationale of parameter manipulation in FRI

We designed and carried out a simulation to compare FRI’s performance on noun and verb generation tasks to that of young subjects, older subjects, and PD patients. The simulation was performed using a simple associative word network and a LISP (Graham, 1995) implementation of the FRI model.

The general parameters of the model were estimated from experimental data (i.e. strength of the associative links, *Sj1i,* see section 5.3.1, equations 1 and 3; and S parameter in equation 2, see appendix 2), from linguistic Italian corpora (i.e. Base rate activation, *Bi,* of equation 1; *fanj2* of equation 2), and through the identification of the best-fitting values for a set of the data, namely the accuracy data of young adults in the noun generation task (i.e. *s* -noise- in equation 4; *F* in equation 5; and a parameter called **delta-w** which gives the degree of shift of attentional weight from one retrieval cue to another after a retrieval failure). Appendix 2 describes the procedure through which these parameters were fixed.

For the rest of simulation, only three parameters which have a specific theoretical and functional significance in the model (i.e. the three executive processes discussed in section 5.3 and reported in figure 5.4) were allowed to vary: *W* (attentional resources allocation, see stage 1 in figure 5.4); *IP* (probability that the retrieved response is checked and eventually inhibited, see stage 3 in figure 5.4); *E* (energization, time needed to recover after a retrieval failure, see figure 5.4).

The *W* parameter was initially set at the value of 1.0 (for young adults), which is the default value in many ACT-R models (Anderson et al., 2004), and was distributed approximately equally to the two activation sources involved in the FRI model (i.e. *Wj1* and *Wj2,* see figure 5.4 and equation 1 in section 5.3.1). Individual differences in working memory capacity and in the ability to differentially activate task-relevant information relative to non-relevant information have been simulated by varying *W* (Daily, Lovett, & Reder, 2001). Accordingly, large values of *W* correspond to an accurate and quick retrieval of goal-relevant information; thus varying *W* does not merely reflect differences in the amount of attentional resources per se, but mirrors diversity in the ability to strategically allocate these resources in order to bias retrieval toward task-relevant information. As we mentioned in section 5.3, in the FRI model we assumed that when retrieval fails more attention is placed on the secondary cue (i.e. increase of *Wj2*), at the expenses of the primary cue (i.e. decrease of *Wj1*). It follows from equation 1 of section 5.3.1 that, the opearation of paying more attention to the secondary cue actually increases the probability of retrieving task-relevant responses (e.g. verbs in verb generation). We varied *W* to mimic differences in such an ability across the three subject populations involved in our simulation.

The Inhibition-Probability (*IP*) parameter controls how frequently the processes of response checking and inhibition intervene in FRI. In fact *IP* is triggered probabilistically in the model, to mimic stochastic fluctuations in the efficiency of inhibitory processes. The larger the values of *IP,* the more preserved is the ability to inhibit unwanted responses. Thus, an IP with a probability = 1 means that a response is always checked and inhibited if wrong (e.g. a noun is inhibited in the verb generation task)[1]. As already shown in section 5.3, after a retrieval failure, another attempt is made to retrieve a correct response. As a consequence, larger values of IP increase RTs and cause more accurate responses (i.e. increase of Wj2 in the second retrieval attempt). The variation in the *IP* parameter was used to capture the potential different extent of inhibition failure in our three populations.

Finally, the *E* parameter was varied to simulate potential differences across populations in the time needed to recover from a retrieval failure (related to the efficiency of the energization process; see footnote 1). Large values of *E* reflect reduced energization; thus, the time to retrieve and produce a response gets longer with larger values of *E*. Each of these three free parameters was allowed to vary only in a direction which mimics a reduction of the respective cognitive resource (i.e., source activation, inhibition efficiency, and energization). Table 5.1 reports the values, obtained by trial and errors, which were assigned to these parameters in the three critical simulations.

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[1] The inhibition-probability (IP) function was defined with the following simple lines of code in LISP:

```
  (defun run-inhibition ()
  (if (>= *IP* (+ 1 (random 100))) 'yes 'no))
```

which means that if a number, randomly selected from 0 to 99 and summed to 1, is smaller than *IP* (which takes a value within the range 1-100) then inhibition works (‘yes), otherwise it does not (‘no). If inhibition works in a given trial, the FRI model checks whether the retrieved response node *i* belongs to the same (syntactic) category of the secondary cue (i.e. a verb is retrived in the context of the verb generation task). If the match is positive the response is produced otherwise it is inhibited and the next retrieval attempt is begun after a time dependent on parameter E (energization). As already shown, successive retrieval attempts involve the variation of both *Wj1* and *Wj2*. On the other hand, if inhibition does not work, no check is made between response nodes *i* and the secondary cue and both correct and incorrect response nodes are produced.

Table 5.1 Final Values of the Free Parameters in the Simulation.

Parameters	Young Participants	Old Participants	PD Participants
W	1	.55	.38
IP	.90	.90	.50
E	.2	.2	3.8

Notes. W is the parameter controlling attentional resources (with a default value of 1 in previous research). IP is expressed as proportion and gives the probability that response checking and inhibition are triggered. E is the time needed to recover from a retrieval failure (in sec). A larger value of W leads to a more accurate and quicker retrieval of task-relevant information. Higher IP values lead to more frequent response checking and inhibition. This increases RTs and is also associated with more accurate responses. An IP of .90 means a 90% of probability for a response node to be inhibited if wrong. Larger values of E reflect reduced energization. The time needed to activate a new retrieval attempt after a failure increases with E. The response deadline in the experimental studies was 4 sec for young and older participants and 6 sec for PD participants.

For each simulation (young adults, older adults, and PD patients) the model was run 15 times across each of the 6 experimental conditions (LS-SA; HS-WA; HS-SA verb and noun generation) for a total of more than 2000 trials (i.e. 15x23x6, with 23 being the number of stimuli in each condition). The mean RT and accuracy performance of the FRI model in each condition of the two tasks was calculated and confronted with that of the three subject populations.

5.4.2. Results

The results of the simulation are summarized in Figures 5.5 (young adults), 5.6 (older adults), and 5.7 (PD patients). The model was able to simulate participants' performance accurately, capturing quite a complex pattern of results on two different tasks in three different populations. Each simulation result falls within the 95% confidence intervals computed from the data, with the single exception of a small underestimation of older participants' errors in the noun generation task. Quantitative measures, computed on 18 data points, confirm the good fit of the model to accuracy data (R^2 = .94 and *RMSD* = 0.049) and RT data (R^2 = .95 and *RMSD* = 0.127 s). These results are satisfying, considering that only three parameters were allowed to vary in a specific direction.

As shown by the inspection of parameter values (Table 5.1), in order to fit young subjects' data the *W* parameter was fixed at its default value; the value of the *IP* parameter allowed that a response was checked and eventually inhibited 90% of the times, and the *E* parameter was fixed at the value of 0.2.

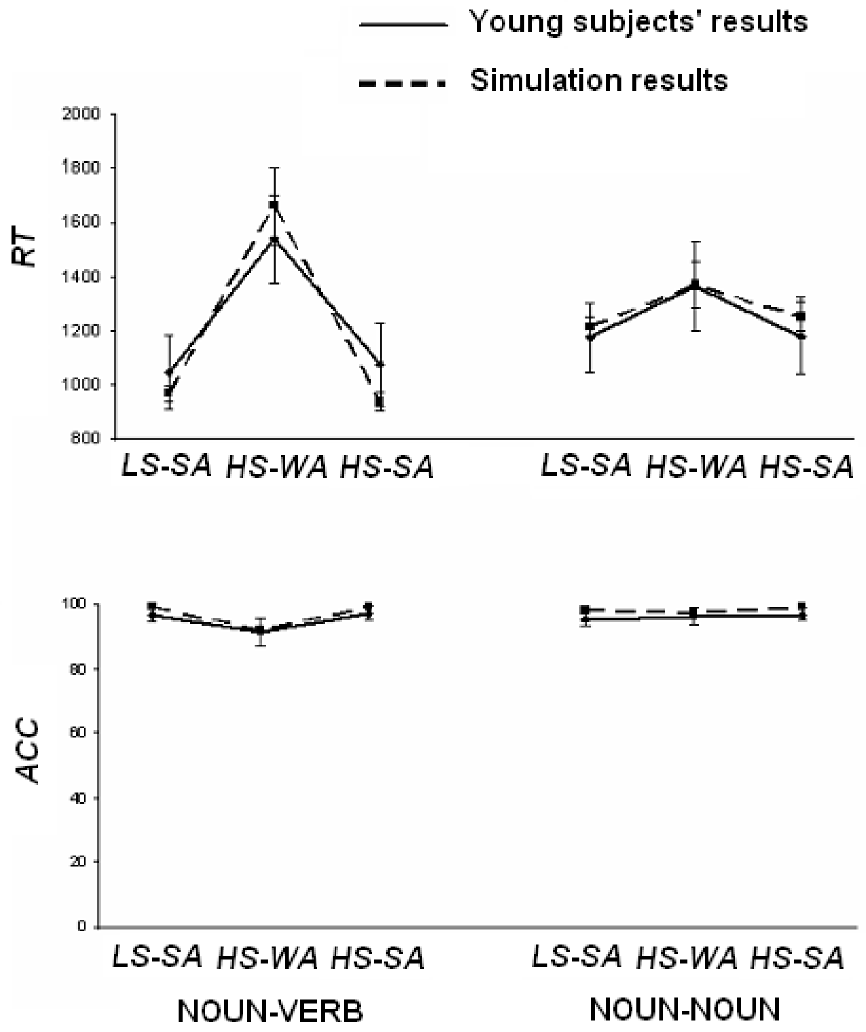

Figure 5.5: Experimental and simulation results for young participants in verb and noun generation tasks, plotted by experimental conditions. The graphs at the top of the figure report response time (RT) performance expressed in msec (verb generation is reported on the left). The graphs at the bottom of the figure report accuracy (ACC) performance expressed as percentage of correct responses (verb generation on the left). Experimental results are presented in solid lines. The averaged simulation results are presented in dotted lines. Noun-Verb and Noun-Noun refer to verb and noun generation respectively. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Error bars indicate 95% confidence intervals.

As far as older subjects' data are concerned, we obtained that the sole reduction of the *W* parameter, which regulated the ability to allocate the available attentional resources for retrieval, was sufficient to fit their data. Except for a minor underestimation of older subjects' errors in the noun generation task, the FRI model was able to accurately replicate the differences that occur between older and young subjects[2].

As shown in chapter 4, older subjects made an equal number of grammatical errors (e.g. a noun is produced in the verb generation task) and no-response errors in the critical HS-WA condition of verb generation; by contrast PD patients made many more grammatical errors than older subjects in the verb generation task and they made this kind of error more often than no-response errors particularly in the HS-WA condition. These different behaviours may suggest that the ability to resist to interference from task-irrelevant responses is more preserved in older subjects than in PD patients. However the higher error-rate and the slower responses in the HS-WA condition of verb generation for older than younger subjects can also indicate a normal physiological effect of aging for such an ability. A decrease of the IP parameter and an increase of the E parameter of the FRI model lead, respectively, to more errors of the kind made by PD patients (i.e. grammatical errors) and to slower RT particularly on the conditions which require more than one retrieval attempt (which we assume to be the HS-WA condition of verb generation). Accordingly, we have tried to fit older subjects' data either by reducing the *IP* parameter while leaving the *W* at the default value of 1, or by mean of a combination of manipulations of both the *IP* and *E* parameters (still leaving unchanged the *W)*. We varied both the two parameters according to a trial and error procedure. Interestingly, FRI was able to fit both accuracy and RT data of the HS-WA condition of verb generation when the *IP* and *E* parameters were assigned the values of 0.60 and 2.0 respectively. However, with these values the model was too much accurate and fast in performing the conditions with strong association of both tasks. In fact, these latter conditions are those that would be less influenced by manipulations of the *IP* and *E* parameters because they suffer less from interference than HS-WA, and thus require less the operations of response inhibition and recovering from retrieval failure. In other words, in older subjects, a value of *W* as in young subjects (i.e. = 1) would guarantee a too much prompt response in the conditions with strong association. Accordingly, a further decrease of *IP* or increase of *E*,

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[2] Old and young subjects' performance can be compared since both subject groups were administered the same paradigm (see figures 5.5 and 5.6). Briefly, as far as global performance on each of the two tasks is concerned, (i.e. merging together RT and accuracy data of the three conditions of each task) older subjects are slower and less accurate than young adults in the verb generation task (RT: t (38) = -2.11, $p < 0.05$; Accuracy: t (38) = 2.62, $p < 0.02$), less accurate in the noun generation task (t (38) = 3.15, $p < 0.01$), and also marginally slower in this latter task (t (38) = -1.97, $p = 0.056$). Further analyses show that the different verb generation performance of the two groups is due to the HS-WA condition. It is only in this condition that older subjects are significantly slower and less accurate than young subjects (RT: t (38) = -3.32, $p < 0.003$; Accuracy t (38) = 3.19, $p < 0.004$). Finally, as far as accuracy performance on the noun generation task is concerned, older subjects are less accurate than young subjects in the two conditions with high selection demands (HS-WA: t (38) = 2.90, $p < 0.008$; HS-SA: t (38) = 3.17, $p < 0.005$) but not in the LS-SA condition ($p = 0.056$).

carried out in the attempt to also fit the data of the strong association conditions, provoked the lack of fit on the HS-WA condition of verb generation for the older subjects' simulation. These results show the crucial role of parameter *W* to fit older subjects' data also of the critical HS-WA verb condition.

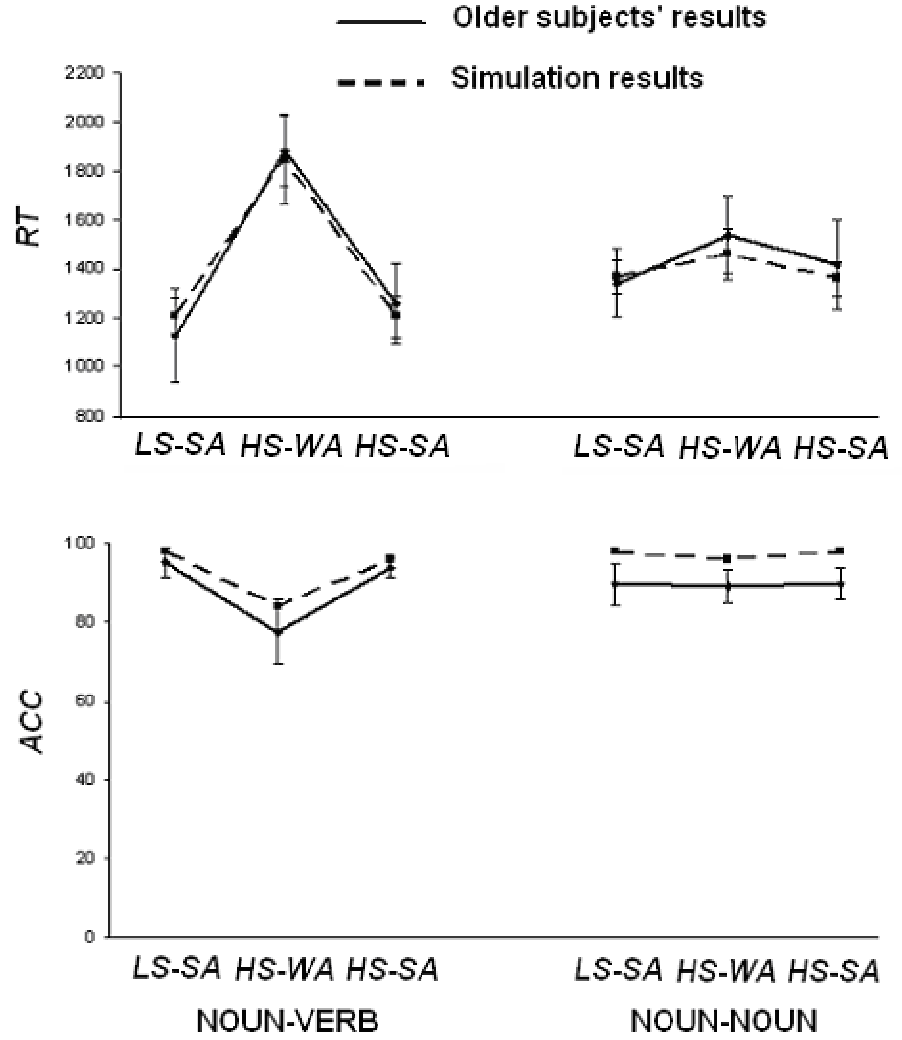


Figure 5.6: Experimental and simulation results for older participants in verb and noun production tasks, plotted by experimental conditions. The graphs at the top of the figure report response time (RT) performance expressed in msec (verb generation is reported on the left). The graphs at the bottom of the figure report accuracy (ACC) performance expressed as percentage of correct responses (verb generation on the left). Experimental results are presented in solid lines. The averaged simulation results are presented in dotted lines. Noun-Verb and Noun-Noun refers to verb and noun generation respectively. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection- Strong Association. Error bars indicate 95% confidence intervals.

Turning now to PD patients' data in chapter 4 we have shown that they performed each condition of the verb generation task worse than older subjects both in terms of RT and accuracy. Moreover, they were also slower than older subjects in each condition of the noun production task. Fitting PD patients' poor generation performance required the manipulation of all three parameters (see table 5.1): a further reduction of the ability to allocate attentional resources (*W*), a diminished probability to inhibit task-irrelevant responses (*IP*), and a much slower recovery from retrieval failures (*E*). In fact, the sole further reduction of the *W* parameter, even at very low values (e.g. 0.25), while leaving the other parameters as in the other two simulations, made FRI too much accurate and fast (relative to PD patients) on most of the conditions of the two tasks, but in particular on the critical HS-WA condition of verb generation. Thus, it appeared necessary to both reduce the ability to inhibit task-irrelevant responses and to increase the time needed for initiating the next retrieval attempt in order to fit the extremely poor performance of PD patients in the verb generation task.

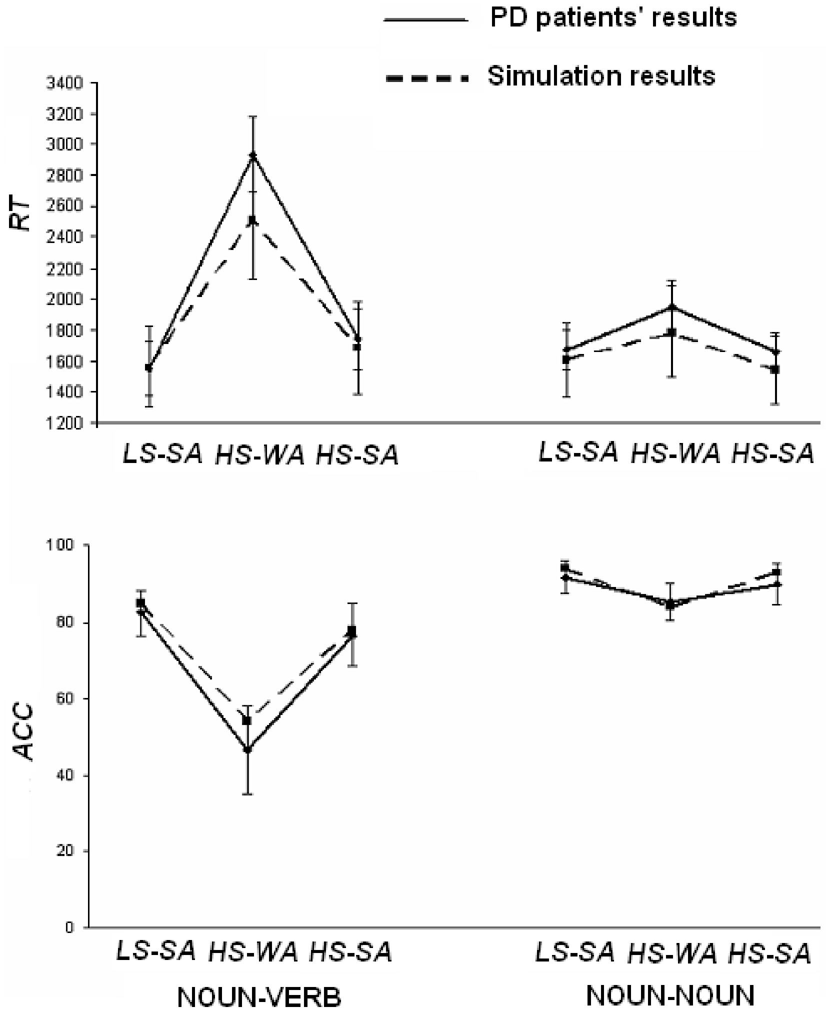


Figure 5.7: Experimental and simulation results for PD patients in verb and noun production tasks, plotted by experimental conditions. The graphs at the top of the figure report response time (RT) performance expressed in msec (verb generation is reported on the left). The graphs at the bottom of the figure report accuracy (ACC) performance expressed as percentage of correct responses (verb generation on the left). Experimental results are presented in solid lines. The averaged simulation results are presented in dotted lines. Noun-Verb and Noun-Noun refers to verb and noun generation respectively. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Error bars indicate 95% confidence intervals.

5.5. General discussion

In this chapter we have reported the results of an experiment of noun and verb generation and described a computational model (FRI) of these two tasks. The model (FRI) was rooted in the ACT-R theory of memory retrieval and on a series of executive control processes; it has similarities with some past accounts of verb generation performance (i.e. Thompson-Schill & Botvinick, 2006; Martin & Byrne, 2006) but, unlike from these, it aims to reproduce and explain in a coherent and unitary framework the performance that both normal and neuropsychological populations (i.e. young adults, older adults, and PD patients) show on tasks of noun and verb generation.

In the FRI model, a cue stimulus initially triggers a pattern of activation over a series of candidate response nodes (i.e. first assumption of Thompson-Schill & Botvinick, 2006); such a pattern of activation can be biased in a task-relevant manner (e.g. toward verb responses) if more attention is strategically allocated to the secondary cue (e.g. “verb”) (Martin & Byrne, 2006; Thompson-Schill & Botvinick, 2006 -third assumption-). Moreover, simple equations derived from the ACT-R memory theory translate the pattern of activation on candidate responses in a single response in our model. Finally, in order to take into account our previous findings on PD patients, the FRI model also implemented a mechanism for dealing with interference from task-irrelevant competitors (Thompson-Schill & Botvinick, 2006). Thus, according to our proposal verb and noun generation consists of (1) strategic allocation of attentional resources on retrieval cues, (2) associative retrieval, (3) and response inhibition. Moreover we have also assumed that the release from a retrieval failure and the initiation of a new retrieval attempt require time and executive resources (energization). A simulation was also carried out in order to test the FRI model on the noun and verb generation tasks and the results have shown that the manipulation of only three theoretically motivated parameters was sufficient to successfully reproduce the performance of all three subject groups.

Experimental and modelling results for young adults’ performance highlight the importance of stimulus-response associative strength for both tasks. Weak stimulus-response associative strength is associated with slower performance than strong associative strength in young adults, in both noun and verb generation. As shown by the activation equation (see equation 1 in section 5.3.1) of ACT-R, a weak stimulus-response associative strength makes a node less active than a strong association. This results in longer response times for less active nodes. The FRI model also mimics young subjects in not showing an effect of selection demands either in response time or accuracy in the two tasks. Indeed, similar values of accuracy and response time were obtained for the two conditions with strong association (i.e. HS-SA = LS-SA). This result confirms the findings of Martin and Cheng (2006) who argued that selection between alternative responses does not play a significant role in verb generation in young adults, at least in situations of strong stimulus-response associative strength. The way in which response selection occurs in ACT-R potentially explains the lack of an effect of selection demands in young adults. In ACT-R (see equation 4 in section 5.3.1) the selection of a response is a probabilistic and competitive process which depends on the level of activation of all competing responses. However, once a response has been selected, more likely that associated with the node with the highest activation, the time needed to produce such a response only reflects its activation level (see equation 5 in section 5.3.1). Both strong stimulus-response associative links and a high level of W (fixed at the default level in young subjects) make the FRI model respond equally fast in the LS-SA and HS-SA conditions.

Young subjects were slower in producing verbs than nouns only in the condition with weak associations (HS-WA), showing a reverse pattern in the other two conditions (i.e. verbs faster than nouns). As we have reported in sections 5.3.1 (see also appendix 2), associative links between secondary cues and their associated nodes are stronger for verbs than nouns. This is represented by the “fan” of activation spreading from secondary cues in FRI and the different activation spreading of noun/verb reflects the fact that the strength of the links between a secondary cue and its associated nodes is inversely proportional to the number of links. Free association norms collected on stimuli indicate that verbs are less represented in the response set than nouns and this explains, in our view, why the concept “verb” spreads more activation on verb responses than does the concept “noun” on noun responses. In our account this difference may give rise, as does in young subjects, to faster verb than noun generation at least in conditions of strong association.

However, the evidence that young adults were slower with verbs than nouns only in the HS-WA condition may confirm our previous claim, based on findings on both older subjects and PD patients, that this condition is the more prone to interference from non-verb competitors. In the FRI model, a weak association between the primary cue and a task-relevant verb response is likely to make this response node less active than a non-verb response associated with the primary cue (free response). In this situation the non-verb response node would be more likely to be retrieved than the task-relevant verb response. Consequently, the task-irrelevant response must be inhibited and another attempt has to be made to recall an appropriate verb response and this has the effect of prolonging response time for verb generation in the HS-WA condition. Thus, the initial advantage of the “fan” of verb responses over noun responses is not sufficient for verbs of the HS-WA condition to overcome the activation of the non-verb responses, which are spontaneously activated by the primary cue. Nevertheless, in the young adults simulation a high value of *IP* and a low value of *E* allow the FRI model to correctly produce verbs in a reasonable time in this critical condition also.

As already mentioned, the FRI model also aimed to reproduce the performance of older subjects and PD patients. As far as the older subjects data are concerned we showed that they were slower and less accurate than young adults particularly in the critical HS-WA condition of verb generation. A reduction of the *W* parameter, that is, of the ability to allocate attentional resources, was sufficient to fit the data of older subjects. As already shown, this parameter has been widely used in ACT-R to simulate individual differences in working memory capacity and in the ability to differentially activate task-relevant relative to task-irrelevant responses (Daily et al., 2001; Anderson et al., 2004). The results of the older subjects simulation support the position that a reduction in the ability to strategically allocate attentional resources may characterize healthy aging (Rogers, 1999), in the domains of executive functions and word retrieval (e.g., Logan, Sanders, Snyder, Morris, & Buckner, 2002; Wierenga et al., 2008).

Thus, in the first of these two studies, Logan et al. (2002) have used fMRI to investigate the mechanisms underlying age-related changes in neural correlates of episodic encoding. In a first experiment the authors asked to both young and older subjects to memorize words and faces for later recall without providing them with any encoding strategy. A strategy was suggested in a specific condition of the second experiment in which subjects were asked to give semantic judgements (abstract vs. concrete words) for each word that was encoded. Logan et al. (2002) found an under-recruitment of frontal regions for older relative to younger subjects in the first experiment; the under-recruitment was, however, reversed when subjects elaborated semantically the material at encoding (second experiment). The authors interpreted these findings suggesting that older adults have problems in the spontaneous recruitment of available frontal resources. In a similar way, in an fMRI study of verb generation based on the paradigm of Thompson-Schill et al. (1997), Persson et al. (2004) have investigated the role of the LIFG in older and younger adults in both conditions of high and low selection. The authors interpreted the finding of a reduced activation in the LIFG for older subjects as due to under-recruitment of resources given that such a reduction was specific for the condition in which the selection requirements were high. Similar findings have been obtained in a more recent fMRI study of word retrieval by Wierenga et al., (2008). This study has shown that age-related differences in word retrieval depend on the difficulty of the retrieval and on the request of manipulation and selection of lexical–semantic information rather than on lexical–semantic knowledge per se which appears to be relatively preserved in healthy aging.

As already shown, PD patients performed the verb generation task very poorly; they had the greatest difficulties on the HS-WA condition of this task in which they produced many nouns instead of verbs. We interpreted this finding as showing that non-verb responses interfere with verb generation particularly in situations of weak association. Consequently, in chapter 4 we have proposed that PD patients are unable to activate the relevant kind of response in verb generation, producing instead task-irrelevant competitors possibly because of a deficit of inhibition. In line with this proposal we obtained that the FRI model was able to fit the PD patients data only when both the *IP* and *W* parameters were manipulated. Fitting PD patients' behavior also required a reduction of the energization process (i.e. an increase of *E*). Accordingly, the FRI model suggests that PD patients have difficulty in copying with highly active task-irrelevant responses. Moreover it also suggests that even when they are able to do so, they are much slower than normal controls in initiating re-allocation of their reduced attentional resources.

Importantly, for the simulation of PD patients the FRI model was also able to reproduce the effects of selection demands which were observed both in RT and in accuracy on the verb generation task. As is suggested by figure 4.2 of chapter 4, the HS-SA condition of verb generation is of slightly higher competition than the LS-SA condition. In fact, in section 4.3.3 –Task-Relevant response-, we have shown that the stimuli of the HS-SA condition elicit less task-relevant responses (i.e. verbs; 7.8% of the response set) than the stimuli of the LS-SA condition (11%; $p = 0.07$). In a similar way, in the FRI model we have obtained that, for verb generation, the difference between the associative strengths of stimulus-task-relevant responses and stimulus-free responses (*Sj1i* in figure 5.4) is larger in the LS-SA than in the HS-SA condition; this confirms that the latter condition is of slightly higher competition than the former. Thus, a non-verb response is more likely to spring to mind in the HS-SA than in the LS-SA condition of verb generation. Accordingly, a reduction of the *IP* parameter (relative to young and older subjects) causes more errors in HS-SA than LS-SA; moreover a reduction of energization and attentional resources also causes prolonged RT for HS-SA in the situations in which a non-verb response is correctly inhibited.

Generally, for the PD patients simulation the interpretation receives support from previous studies, briefly reported in the Introduction of the thesis (see sections 1.2.1 and 1.3), which showed problems in these patients in the strategic allocation of attentional resources (e.g., Robertson et al., 1996), decreased inhibitory control (e.g. Dujardin et al., 1999; Bouquet et al., 2003; Castner et al., 2007), and difficulties in initiating a response after a shift (e.g., Partiot et al., 1996). In the Introduction of the thesis we also discussed that BG structures may be involved in the process of energising responses (e.g. Laplane & Dubois, 2001).

Turning back to the debate on verb generation between the competitive (Thompson-Schill et al., 1997; 1998; Thompson-Schill & Botvinick, 2006) vs. associative strength (Martin & Cheng, 2006; Martin & Byrne, 2006) positions, the FRI model shows that they can be integrated into a unified model. In the model the effects of the competition factor emerge reliably only in PD patients, that is, in the context of poor inhibitory and attentional control and reduced energization. In situations of strong stimulus-response associative strength, this factor reflects specific dynamic of response selection at a relatively early stages of verb/noun generation (e.g. ACT-R associative retrieval module). On the other hand, effects of associative strength emerge more consistently across populations and in both tasks. They are particularly evident in the weak association condition of verb generation and are due to the interference caused by task-irrelevant competitors. In fact, it is predominantly in this situation (i.e. weak association) that both response inhibition and prompt re-allocation of attention are critical for successful performance. Thus the two original positions (i.e. competition and associative strength) are not alternative accounts or alternative viewpoints on the same thing as has been proposed.

Finally, as already mentioned, our proposal also confirms recent evidence (e.g. Bouquet et al., 2003; Castner et al., 2007) which shows that the pathophysiology of PD may affect different processes of the SAS system (Norman & Shallice, 1986). Our results show that a number of deficits may give rise to the neuropsychological profile of patients with PD, and that these deficits, although contributing to the language generation difficulties of the patients, may not be specific to this cognitive domain. Thus, our model indicates that the BG have an important role in the processes of response selection and inhibition as well as in energizing schemata and more generally that fronto-striatal circuits are important for allocating attentional resources strategically in order to bias retrieval in a task-relevant manner.

Summarizing, we have proposed a unitary account for the main experimental findings, relying on an associative theory of retrieval (ACT-R) complemented by specific control processes (allocation of attention on retrieval cues, response checking and inhibition, energization). Simulation results have shown that this account can represent a good integrative explanation for the performance of young, older, and PD participants on tasks of noun and verb generation.

Chapter 6

6.1. Aim of the functional magnetic resonance imaging (fMRI) study of noun and verb generation

The findings reported in chapter 4 have shown that both the factors of stimulus-response association strength and of selection between competing alternatives are important in determining whether a response can be produced in PD patients. Consistently with these results, the findings reported in chapter 5 have suggested that both the accounts of verb generation in terms of strength of stimulus-response association and selection between alternative responses can be integrated into one coherent model. Of importance, both the study carried out on PD patients (chapter 4) and the Focus-Retrieve-Inhibit (FRI) model (chapter 5) indicate that association strength effects are particularly evident on the HS-WA condition of verb generation. We have argued that this is the case because both the needs to resist to interference from task-irrelevant responses (i.e. noun responses) and of energizing a task-relevant type of response are higher in the HS-WA condition of verb generation than in both the corresponding condition of noun generation and the strong association conditions of both tasks (i.e. LS-SA and HS-SA noun/verb generation). Moreover, the strikingly poor performance of PD patients on the HS-WA condition of verb generation strongly suggests that basal ganglia (BG) may be crucially involved in this condition.

Nevertheless, the left inferior frontal gyrus (LIFG) has been seen to be primarily involved in single word generation tasks. As already shown, previous neuropsychological and neuroimaging studies explored the cognitive and neural substrates involved in verb generation emphasising a role for the LIFG either of response selection between competing alternatives (Thompson-Schill et al., 1997; 1998; Persson et al., 2004) or of semantically controlled retrieval (Wagner, Paré-Blagoev, Clark, & Poldrack, 2001; Martin & Cheng, 2006; Danker et al., 2008). Interestingly, Badre et al. (2005) have recently attempted to reconcile the selection and association strength accounts, providing fMRI evidence of some functional segregation within the LIFG. Subjects were presented with a noun-cue and they had to choose one stimulus between two to four possible targets. In different conditions, the association strength between target and the cue was either strong or weak; or the selection requirement was high or low (e.g. two versus four possible targets). The results revealed that the left mid-ventro lateral prefrontal cortex (VLPFC, inferior frontal gyrus pars triangularis and pars opercularis, BA 44/45) was activated in the high selection vs. low selection conditions, while the more anterior/ventral section (including the inferior frontal gyrus pars orbitalis, BA 47) activated during controlled retrieval (weak vs. strong association conditions). Nonetheless, it should be noted that none of the conditions presented in this study required the subjects to generate target words, thus the results may not apply fully to word generation tasks.

The aim of the current fMRI study is to dissociate response selection and association strength during single word generation and to investigate the role of these two factors in the activation of frontal-striatal circuits. We have used the same tasks of verb and noun generation as those previously administered to our subject populations (i.e. young subjects, older subjects, and PD patients) in order to investigate possible commonalities and differences for these two types of stimuli. Furthermore, we recorded overt vocal responses during fMRI, which enabled us to monitor word generation performance on each trial.

We investigated the effect of selection by comparing high-selection versus low-selection conditions, with matched association strength (i.e. “at least two” versus “just one” possible response; HS-SA > LS-SA); and the effect of association strength by comparing weak versus strong conditions, with equalised selection demands (i.e. two weakly associated responses versus two strongly associated responses; HS-WA > HS-SA). It should be noted that selection and association cannot be manipulated in fully factorial manner, because there are effectively no cue-words to act as triggers in a “low selection & weak association” condition (cf. also Martin & Cheng, 2006). Therefore our analyses can only compare relevant conditions pairwise (e.g. high versus low selection), but critically avoiding any confounding effect of the other factor (i.e. the level of association strength, in this example).

We expected that high selection demands would activate the mid-LIFG during verb generation (Thompson-Schill et al., 1997; 1998; Barch et al., 2000; Persson et al., 2004; see also, in chapter 4, the effect of selection demands on RT in older subjects and PD patients); and we assessed here for the first time the role of selection during noun generation. As far as the effect of association strength is concerned, we hypothesised that there could be a possible involvement of the more anterior section of the left VLPFC in the weak association condition following Badre et al. (2005), but now using active word generation tasks rather than merely target discrimination. Finally, following our previous results in PD patients we predict increased activation in basal ganglia for the weak association condition, specifically during verb generation. This would support the hypothesis that the BG play a critical role in situations when noun competitors interfere with the production of weakly associated verbs.

6.2. Materials and Methods of the study

6.2.1. Participants

Fourteen right-handed healthy volunteers (6 males, 30.5 ± 4.5 years) participated in the study. All participants had no existing neurological or psychiatric illness. All subjects gave written informed consent, and the study was approved by the independent Ethics Committee of the Fondazione Santa Lucia (Scientific Institute for Research Hospitalisation and Health Care, Rome).

6.2.2. Design

The design of the current fMRI experiment was based both on the previous behavioral study of Martin and Cheng (2006) and on our studies (see chapters 4 and 5). Accordingly, we tested for the effect of response selection comparing two conditions that differed for selection demands, but were equated for association strength: Low Selection-Strong Association (LS-SA) and High Selection-Strong Association (HS-SA); and we tested for the effect of association comparing two conditions with different levels of association strength, but with the same selection demands: High Selection-Weak Association (HS-WA) and High Selection-Strong Association (HS-SA). In addition, our design included both verb and noun generation tasks, allowing us to investigate the effects of selection and association in two different types of generation tasks. A baseline "READ" condition was also included. This permitted us to investigate brain activation common to the verb and the noun tasks (irrespective of selection and association conditions), but without any trivial confounds related to common low-level sensory-motor processes (e.g. processing of the sensory cue, overt vocalization, etc).

6.2.3. Stimuli

The same stimuli were used as in our previous studies. There were three experimental conditions varying in selection demands and mean association strength. As a measure of selection demand for each stimulus, we used the ratio of the response frequencies of the two most common responses to that stimulus (following Thompson-Schill et al., 1998). The measure of stimulus-response association strength for each stimulus was calculated as the ratio of the mean associative strength of the two most frequent responses to the number of subjects who judged noun-verb (and noun-noun) stimuli (see chapter 4, for further details on the procedure used to collect all stimuli). Thus in two experimental conditions, the stimuli were matched for stimulus-response associative strength but differed in selection demands (e.g. low selection: LS-SA vs. high selection: HS-SA). The third experimental condition consisted of stimuli with high selection demands and weak stimulus-response associative strength (HS-WA) (see chapter 4 for some specific examples of stimuli).

The stimuli in the three conditions of verb generation were matched for the strength of the first non-verb response given during free association. Moreover, as already shown in chapter 4, in both tasks the two conditions with strong associations (LS-SA and HS-SA) did not differ in the number of task-relevant responses that were produced in situations of free association (e.g. the number of verbs produced in the verb generation task), but this value was significantly higher than that in the conditions with weak association (HS-WA) (see figure 4.2 of chapter 4).

6.2.4. Procedure

Figure 6.1 reports a schematic representation of the experimental procedure. Before fMRI scanning the participants practiced the tasks during a 5-min training session. During practice they were shown six blocks of stimuli, each consisting of four noun stimuli, each of which appeared on the computer screen at 4-s intervals. There were two “Read” blocks in which the stimuli had to be read by the subjects and two blocks for each of the two experimental tasks (noun and verb generation). The order of the blocks for the practice session was fixed: *Read-Noun Generation-Verb Generation,* repeated twice. During practice, subjects were instructed on how to produce spoken responses while moving the face muscles as little as possible.

In the scanning session, the participants were asked to generate a verb (or a noun) related to a visually presented noun or to read the noun stimulus. For each noun the participants responded aloud. The nouns were presented for 1s each; vocal responses were recorded during 3.5s starting from the presentation of the stimulus (intertrial interval = 4-5 s). After the stimulus disappeared from the screen a fixation cross appeared. Noun stimuli were grouped in blocks of four. Thus, each block lasted approximately 20-s. At the beginning of each block an instruction was presented for 1500 ms informing the subjects about the upcoming task. A group of eight blocks formed one presentation of an experimental task. Blocks within a group alternated according to a balanced Latin Square design. In each group, six of the eight blocks were formed by stimuli of the three experimental conditions (two blocks per condition) while the remaining two blocks consisted of “Read” stimuli. In total, each group of eight blocks consisted of 32 stimuli.

The study was divided into two fMRI runs, each of these consisted of four groups of eight blocks (two groups per experimental task, see figure 6.1). The order of repetition of the two tasks was counterbalanced across subjects; for half of the participants the order was: *Noun-Verb-Verb-Noun* for the first run and *Verb-Noun-Noun-Verb* for the second run. For the second half of the subjects it was: *Verb-Noun-Noun-Verb*, first run, and *Noun-Verb-Verb-Noun* for the second run. For the generate tasks (noun or verb) participants were not informed of the different conditions (LS-SA, HS-WA, HS-SA). Before the beginning of the fifth block and at the end of the last block of each group of eight blocks there were *Rest* periods of 20-s during which a fixation cross appeared on the screen. The total time of the fMRI-session was approximately of 27 min (2 fMRI-runs of 13.5 min each).

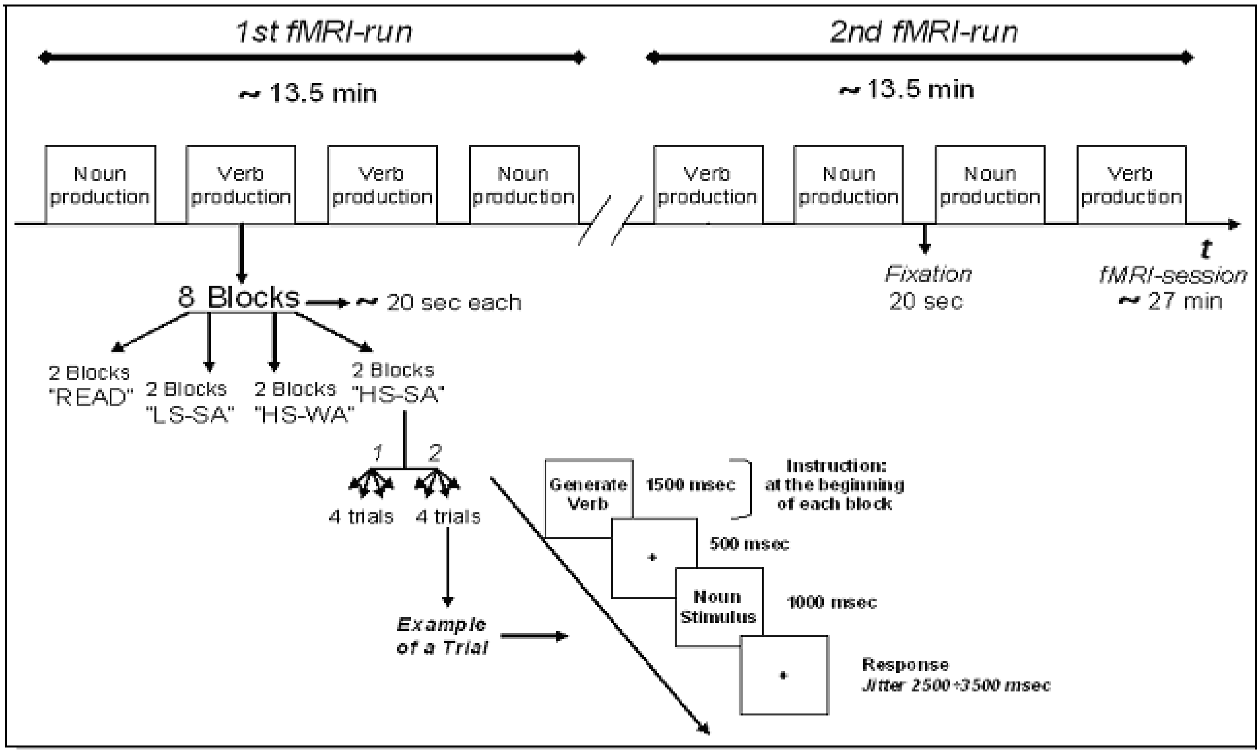


Figure 6.1: Experimental design. The timing of the events in a trial is also reported. READ indicates the baseline condition in which noun stimuli have to be read. LS-SA stands for Low Selection-Strong association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. See main text for further details.

6.2.5. Verbal response recording

In order to acquire overt verbal responses we used a method similar to that of Barch et al. (2000). A plastic tube was fixed to the headcoil through a plastic funnel and taped, outside the scanner room, to a microphone that was in turn attached to a computer. The plastic tube was used to allow placement of the microphone outside the bore of the scanner.

Each subject’s response was recorded as a *.wav* file. The *Noise Reduction* facility of Cool Edit Pro. 2.00 (Syntrillium Software Corporation, Phoenix, USA) was used to isolate a subject’s response from the scanner noise. The responses were transcribed and checked for accuracy and reaction times were calculated from the onset of the stimulus to the onset of the subject's response. For all 14 subjects, almost all responses that were produced were recorded clearly. Most of the errors made by the subjects were missed responses; in a few cases they did not pay attention to the instructions and, for entire blocks of stimuli, generated nouns when verbs were required or verbs when noun generation was the task at hand. Nevertheless, subjects' behaviour indicated that they generally carried out the tasks appropriately. Both behavioural and imaging data are referred to subjects' correct responses only.

6.2.6. fMRI methods

Images were acquired using a 3-T MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with a standard quadrature headcoil and for echo-planar imaging (EPI). Head movement was minimized by mild restraint and cushioning. Thirty-two slices of functional MR images were acquired using blood oxygenation level-dependent imaging (3 x 3 mm, 2.5 mm thick, repetition time = 2.08 s, time echo = 30 ms), covering the entirety of the cortex. At the end of the scanning session, anatomical scans were also acquired for each subject, using a T1-weighted MP-RAGE (magnetization-prepared, rapid acquisition gradient echo).

Experimental tasks were presented using Cogent 2000 (developed by the Cogent 2000 team at the FIL and the ICN, London). SPM5 (Wellcome Department of Cognitive Neurology, see Friston, 2004) was used for data preprocessing and statistical analyses. For all participants we acquired 792 volumes (396 each fMRI-run); the first 4 of these were discarded for each run. All images were then corrected for head movement. Slice-acquisition delays were corrected using the middle slice as reference. All images were normalized to the standard SPM5 EPI template and spatially smoothed using an 8 mm FWHM Gaussian filter. All images were high-pass filtered at the cutoff value of 128-s.

All subsequent analyses of the functional images were performed using the general linear model implemented in SPM5. First, for each subject, the data were fitted at every voxel using a combination of effects of interest. The onset of each trial of the eight conditions (READ, LS-SA, HS-WA, and HS-SA for noun generation and READ, LS-SA, HS-WA, and HS-SA for verb generation) was convolved with the hemodynamic response function (HRF). For each condition, the data were modelled as event-related (duration = 0) considering only trials with correct response. Error trials were modelled with a separate regressor and excluded from subsequent group-level analyses. Indeed, as covariates of no interest, both the parameters of the realignment (motion correction) and the onset of each error-trial were also included in the design matrix. We then obtained 6 contrast images per subject subtracting the READ condition form each of the 6 conditions of interest (LS-SA, HS-WA, HS-SA noun and verb generation). These 6-contrast images per subject underwent an analysis of variance (ANOVA) for group-level random effects statistical inference. Correction for nonsphericity (Friston et al., 2002) was used to reduce for any non-independent error terms in the repeated measures analysis. All reported activations survived a whole-brain *P* corrected = 0.05 (cluster level, estimated at p-uncorrected threshold < 0.001). In addition, one-sample t-tests were used to compare pairwise: *noun generation vs. fixation, and verb generation vs. fixation* (p-corr. = 0.05, cluster level).

6.3. Results

6.3.1. Behavioral data

Response time analyses

The results of noun and verb generation tasks are shown in Figure 6.2. Reaction times data did not violate assumptions of normality (all Shapiro-Wilk p values > .2). A 2 x 3 repeated measures ANOVA with task (noun and verb generation) and condition (LS-SA; HS-WA; HS-SA) as within-subject factors was carried out on RT. The analysis showed the main effect of task (F (1, 13) = 7.12, p < .02), the main effect of condition (F (2, 26) = 104.38, p < .001) and a significant taskXcondition interaction (F (2, 26) = 34.85, p < .001). The main effect of task arose from verb generation which was globally performed faster than noun generation. In view of the significant interaction two repeated measure ANOVAs were carried out, one for each task. These analyses gave a significant main effect of condition both for noun generation (F (2, 26) = 8.17, p < 0.01) and for verb generation (F (2, 26) = 128.42, p < 0.001). Post-hoc pair-wise contrasts carried out for the noun generation task showed significant differences (using Bonferroni corrections) between LS-SA vs. HS-WA (F (1, 13) = 10.00, uncorrected p < 0.008) and HS-SA vs. HS-WA (F (1, 13) = 11.94, uncorrected p < 0.005) but no difference between LS-SA vs. HS-SA (F (1, 13) = 0.01, p = 0.91). The data show a clear effect of association strength but not of selection demands for RT in noun generation. Post-hoc pair-wise contrasts executed for the verb generation task showed a similar pattern of results: significant differences (using Bonferroni corrections) for comparisons between LS-SA vs. HS-WA (F (1, 13) = 121.54, uncorrected p < 0.001) and HS-SA vs. HS-WA (F (1, 13) = 196.79, uncorrected p < 0.001), but unlike noun generation, there was also a difference between LS-SA vs. HS-SA (F (1, 13) = 11.95, uncorrected p < 0.005). Effects of association strength and selection demands are present in the verb generation task.

In view of the interaction we also performed post-hoc pair-wise contrasts (Bonferroni correction applied) between pairs of corresponding conditions of the two tasks. These contrasts showed that verbs were produced faster than nouns in the conditions with strong association (verb-LS-SA vs. noun-LS-SA, F (1, 13) = 21.47, uncorrected p < 0.001; verb-HS-SA vs. noun-HS-SA, F (1, 13) = 34.02, uncorrected p < 0.001). However, in line with the findings of chapters 4 and 5, verb generation was marginally slower than noun generation in the critical condition with weak association (verb-HS-WA vs. noun-HS-WA, F (1, 13) = 6.45, p < 0.25).

Finally two t-tests showed that the "read" condition was performed faster than both the two generation tasks (read vs. verb: t = -16.55 (13), p < .001, read: *M* = 794 msec, verb: *M* = 1585 msec; read vs. noun: t = -25.87 (13), p < .001, read: *M* = 794 msec, noun: *M* = 1676 msec).

Accuracy analyses

The results of noun and verb generation tasks are shown in Figure 6.2. Using Shapiro-Wilk tests of normality four out of seven of the accuracy distributions (6 experimental conditions plus the Read condition) were not normal. An arcsine transformation was performed on the data. Following the transformation only the accuracy distribution of the Read condition was well below the threshold for normality.

A 2 x 3 repeated measures ANOVA with task (noun and verb generation) and condition (LS-SA; HS-WA; HS-SA) as within-subject factors was carried out on the proportion of correct responses. The analysis showed a significant effect of condition (F (2, 26) = 32.44, p < .001) and a significant taskXcondition interaction (F (2, 26) = 6.20, p < .01), but the main effect of task was not significant (F (1, 13) = 0.16, p = .68).

In view of the significant interaction two repeated measure ANOVAs were carried out, one for each task. These analyses gave a significant main effect of condition both for noun generation (F (1, 13) = 14.46, p < 0.001) and for verb generation (F (1, 13) = 29.80, p < 0.001). Post-hoc pair-wise contrasts executed for the noun generation task showed significant differences (using Bonferroni corrections) between LS-SA vs. HS-WA (F (1, 13) = 19.64, uncorrected p < 0.001) and HS-SA vs. HS-WA (F (1, 13) = 20.51, uncorrected p < 0.001) but no difference between LS-SA vs. HS-SA (F (1, 13) = 0.57, p = 0.46). The data show a clear effect of association strength but not of selection demands for accuracy in noun generation.

Post-hoc pair-wise contrasts executed for the verb generation task showed an analogous pattern of results: significant differences (using Bonferroni corrections) for comparisons between LS-SA vs. HS-WA (F (1, 13) = 36.18, uncorrected $p < 0.001$) and HS-SA vs. HS-WA (F (1, 13) = 31.61, uncorrected $p < 0.001$), but no difference between LS-SA vs. HS-SA (F (1, 13) = 1.60, p = 0.23). An effect of association strength but not of selection demands was also present in the verb generation task.

In view of the interaction we also performed post-hoc pair-wise contrasts (Bonferroni correction applied) between pairs of corresponding conditions of the two tasks. These contrasts showed a trend of verb generation performed better than noun generation for the LS-SA condition (verb-LS-SA vs. noun-LS-SA, F (1, 13) = 5.28, corrected p = 0.039) and no difference between tasks for both the HS-SA condition (verb-HS-SA vs. noun-HS-SA, F (1, 13) = 0.60, p = 0.45), and the HS-WA condition (verb-HS-WA vs. noun-HS-WA, F (1, 13) = 2.11, p = 0.17). Finally, Wilcoxon tests showed that the “read” condition was performed better than both the two generation tasks (read vs. verb: Z = -3.18, $p < .01$, read: *M* = .98, verb: *M* = .91; read vs. noun: Z = -3.19, $p < .01$, read: *M* = .98, noun: *M* = .91).

The behavioural data confirm the findings reported in previous chapters (4 and 5) and show that the weak association conditions lead to longer reaction times and are associated with poorer performance than the conditions with strong association. In addition, a selection demands effect is found in the response time data of the verb production task. Finally, verb generation is slower than noun production in the weak association condition but faster in situations of strong association.

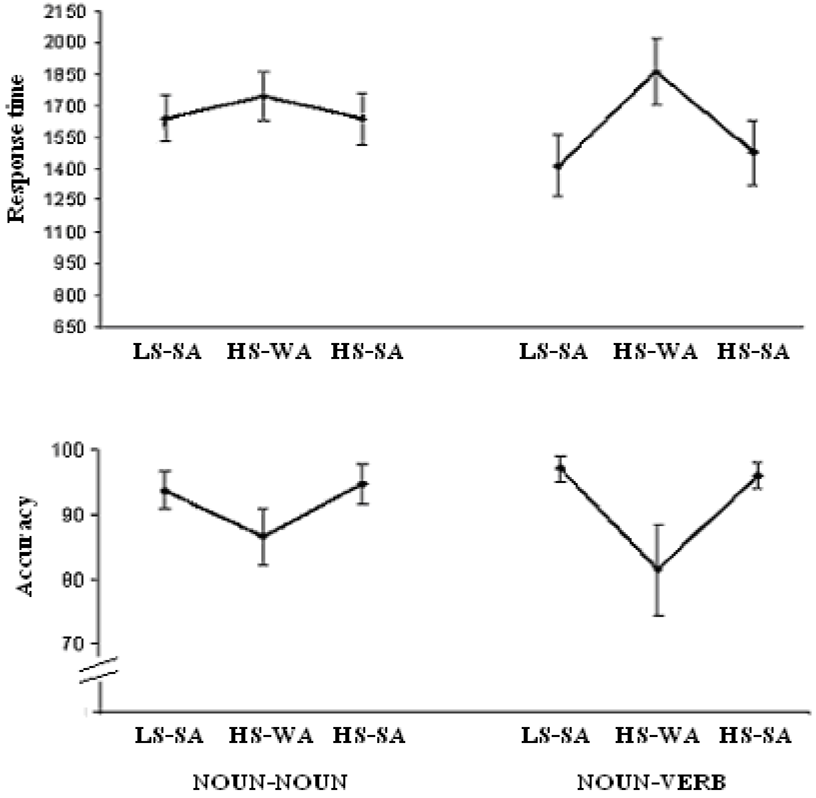


Figure 6.2: Behavioral results. The graphs at the top of the figure report response time (msec) performance on noun (left) and verb (right) generation tasks. The graphs at the bottom of the figure report accuracy performance (%) in both tasks (noun generation on the left). LS-SA stands for Low Selection-Strong association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association. Bars indicate standard deviation.

6.3.2. Neuroimaging data

6.3.2.1. Noun generation vs. fixation and verb generation vs. fixation

First of all, both tasks were contrasted with a fixation condition. The contrast noun generation vs. fixation resulted in the activation of six clusters (see Table 6.1). There was a posterior cluster with the peak activation located in the left middle occipital gyrus. A second large cluster involved the left inferior frontal gyrus and extended to the left middle frontal gyrus, left precentral gyrus, left insula, left putamen and left superior temporal gyrus. In addition, the anterior cingulate cortex and the superior frontal gyrus were activated as part of another cluster. As for the condition of noun generation, the largest cluster activated by verb generation, relative to fixation, was located in posterior brain areas. Another cluster activated by verb generation included the left inferior frontal gyrus, left precentral gyrus, left insula, left and right putamen, left superior temporal gyrus, left and right substantia nigra, left and right thalamus, and right nucleus caudate (see Table 6.1).

Table 6.1.
Noun generation vs. fixation and verb generation vs. fixation

Anatomical localization	MNI coordinates			P corrected	Z Value	Voxels per cluster
	x	y	z			
Regions more active for nouns vs. fixation						
L Middle occipital gyrus	-30	-92	18	< 0.001	5.70	10515
L Cuneus	-20	-98	8	< 0.001	5.03	
R Cuneus	18	-102	6	< 0.001	4.24	
L Fusiform gyrus	-38	-50	-24	< 0.001	4.84	
R Fusiform gyrus	32	-82	-14	< 0.001	4.03	
L Lingual gyrus	-10	-68	-2	< 0.001	4.14	
R Lingual gyrus	14	-96	-14	< 0.001	4.24	
R Cerebellum	36	-62	-32	< 0.001	4.60	
R Middle occipital gyrus	28	-98	10	< 0.001	4.47	
L Superior occipital gyrus	-22	-94	28	< 0.001	3.84	
L Inferior occipital gyrus	-44	-70	-16	< 0.001	4.27	
L Inferior temporal gyrus	-52	-64	-18	< 0.001	4.06	
L Inferior frontal gyrus	-46	4	42	< 0.001	6.12	7509
L Middle frontal gyrus	-46	0	56	< 0.001	5.22	
L Precentral gyrus	-52	-12	40	< 0.001	5.20	
L Insula	-32	18	6	< 0.001	5.02	
L Putamen	-22	10	0	< 0.001	4.66	
L Superior temporal gyrus	-54	14	-4	< 0.001	4.11	
L Anterior cingulate cortex	-8	24	42	< 0.001	3.85	1607
L Superior frontal gyrus	-14	0	72	< 0.001	3.15	
R Precentral gyrus	46	-12	34	< 0.001	5.03	1490
R Putamen	22	12	2	< 0.003	4.11	350
L Superior parietal lobule	-26	-60	52	< 0.005	4.80	308
Regions more active for verbs vs. fixation						
L Middle occipital gyrus	-22	-98	12	< 0.001	5.76	17586
R Middle occipital gyrus	34	-94	2	< 0.001	5.36	
L Superior parietal lobule	-26	-60	56	< 0.001	5.64	
L Cuneus	-4	-94	24	< 0.001	5.20	
R Cuneus	10	-80	8	< 0.001	5.09	
L Fusiform gyrus	-40	-50	-24	< 0.001	5.21	
R Fusiform gyrus	30	-68	-20	< 0.001	5.16	
L Lingual gyrus	-20	-92	-12	< 0.001	5.26	
R Cerebellum	36	-62	-34	< 0.001	5.54	
L Inferior frontal gyrus	-40	4	40	< 0.001	5.89	11265
L Precentral gyrus	-50	-12	38	< 0.001	5.71	
L Insula	-32	22	2	< 0.001	5.32	
L Putamen	-22	8	-4	< 0.001	5.81	
R Putamen	24	10	0	< 0.001	5.01	
L Superior temporal gyrus	-56	12	-10	< 0.001	4.86	
L Substantia Nigra	-6	-20	-16	< 0.001	4.60	
R Substantia Nigra	8	-18	-14	< 0.001	4.57	
L Thalamus	-10	-14	8	< 0.001	4.12	
R Thalamus	14	-18	0	< 0.001	3.64	
R Nucleus caudate	28	-6	-12	< 0.001	3.47	
L Middle frontal gyrus	-6	16	54	< 0.001	6.16	2267
L Superior frontal gyrus	-14	0	72	< 0.001	4.86	
L Anterior cingulate cortex	-10	24	40	< 0.001	4.55	
R Precentral gyrus	50	-10	32	< 0.001	5.48	1768
R Superior temporal gyrus	52	-22	-2	< 0.001	4.66	501
L Middle temporal gyrus	-66	-28	2	< 0.002	4.39	353

Notes: Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $P < 0.05$ corrected, estimated at $p < 0.001$ uncorrected) given in millimeter with effect sizes (*z* scores) and cluster extent. In the Voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas and then selecting peaks within each area.

6.3.2.2. Noun generation vs. read, verb generation vs. read, and Verb vs. Noun

Table 6.2 and figure 6.3 report the brain areas that were more active for noun and verb generation relative to the read condition.

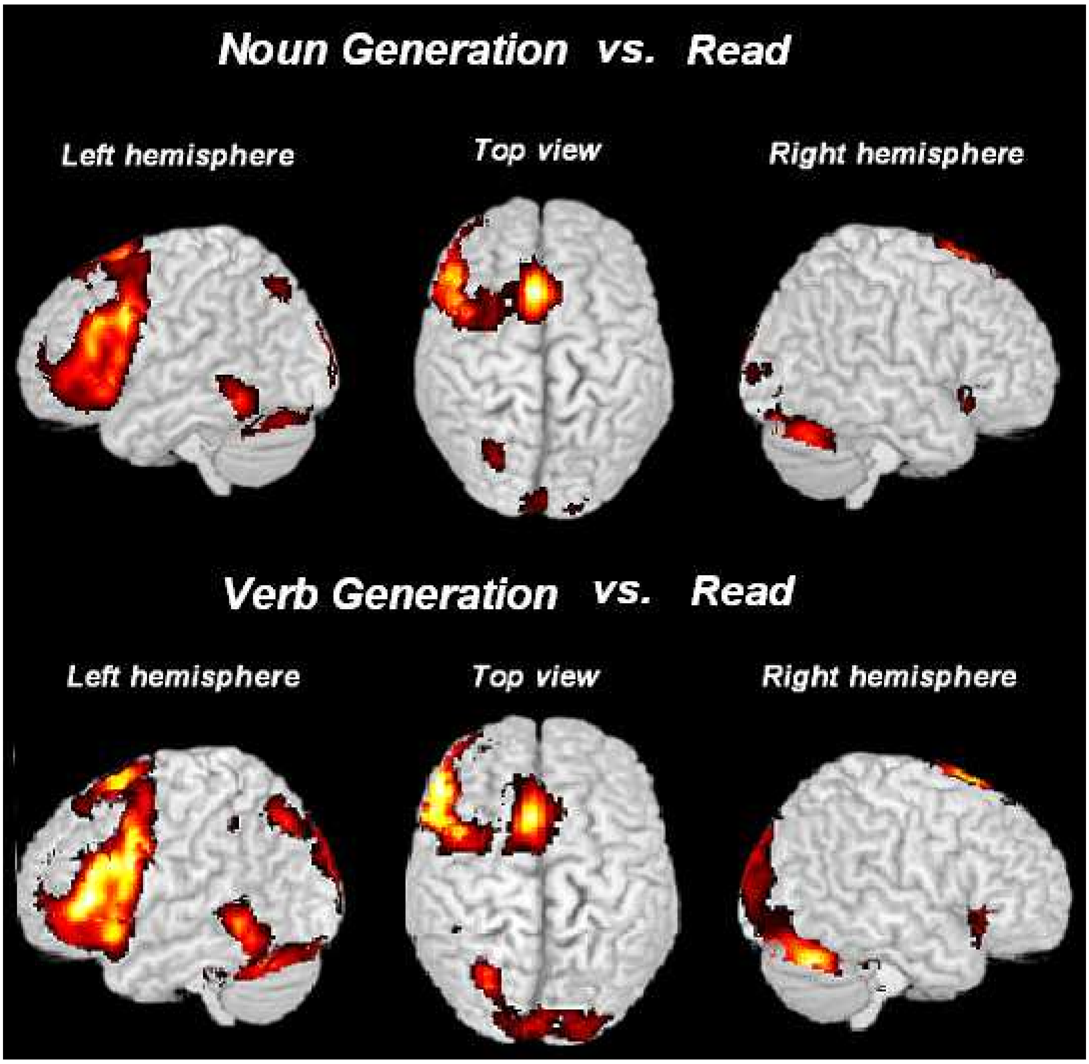
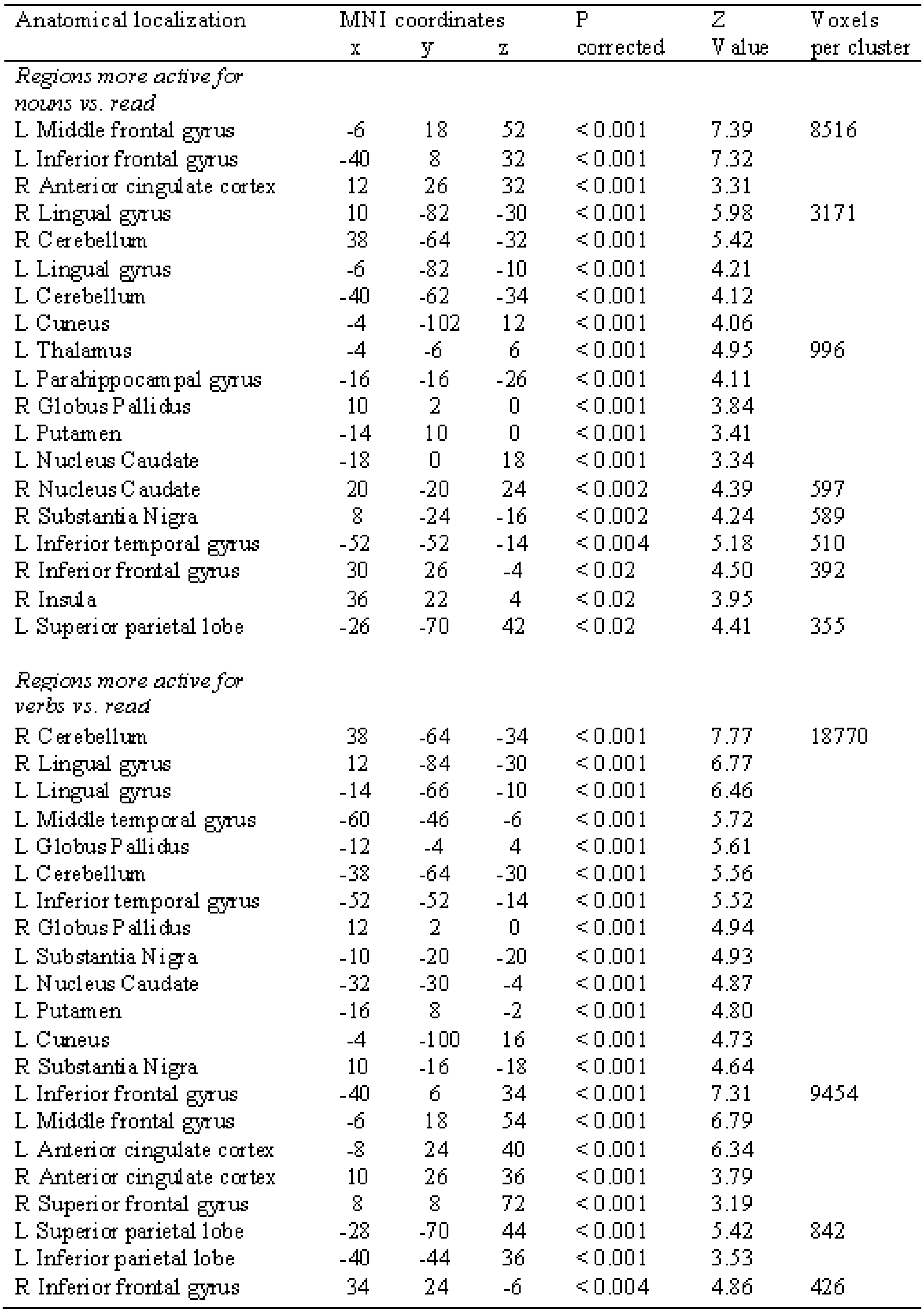


Figure 6.3: Brain activation for the contrasts noun generation vs. read (top), and verb generation vs. read (bottom).

The comparison of noun generation with the read condition revealed activation of a large network of brain areas. The strongest activations involved the left middle and inferior frontal gyri and the anterior cingulate cortex. Activation was also found in the lingual gyrus, the left cuneus and cerebellum (bilaterally). Moreover, subcortical areas such as nucleus caudate (bilaterally), left thalamus and putamen, and right substantia nigra and globus pallidus were also more active for nouns than read (see table 6.2). The largest cluster activated during verb generation relative to read involved posterior brain regions and subcortical areas; thus, in this cluster the cerebellum, lingual gyrus, globus pallidus, and the substantia nigra were activated bilaterally, whereas the middle temporal gyrus, inferior temporal gyrus, nucleus caudate, putamen, and cuneus were lateralized on the left. Moreover, the left inferior and middle frontal gyri, anterior cingulate cortex, and the right superior frontal gyrus were activated as part of a different cluster.

The two generation tasks were also contrasted directly against each other. No brain regions were more active for nouns than verbs. By contrast, the contrast Verb > Noun led to the activation of the left superior and middle temporal gyri (see first contrast of table 6.3 and the bottom part of figure 6.4). The activation plots of the bottom part of figure 6.4. report activation in these temporal regions for each condition of the two tasks. The signal plots indicate that verb generation activates these regions in a similar way to the read condition.

Table 6.2.
Noun generation vs. read and verb generation vs. read



Anatomical localization	MNI coordinates x	y	z	P corrected	Z Value	Voxels per cluster
Regions more active for nouns vs. read						
L Middle frontal gyrus	-6	18	52	< 0.001	7.39	8516
L Inferior frontal gyrus	-40	8	32	< 0.001	7.32	
R Anterior cingulate cortex	12	26	32	< 0.001	3.31	
R Lingual gyrus	10	-82	-30	< 0.001	5.98	3171
R Cerebellum	38	-64	-32	< 0.001	5.42	
L Lingual gyrus	-6	-82	-10	< 0.001	4.21	
L Cerebellum	-40	-62	-34	< 0.001	4.12	
L Cuneus	-4	-102	12	< 0.001	4.06	
L Thalamus	-4	-6	6	< 0.001	4.95	996
L Parahippocampal gyrus	-16	-16	-26	< 0.001	4.11	
R Globus Pallidus	10	2	0	< 0.001	3.84	
L Putamen	-14	10	0	< 0.001	3.41	
L Nucleus Caudate	-18	0	18	< 0.001	3.34	
R Nucleus Caudate	20	-20	24	< 0.002	4.39	597
R Substantia Nigra	8	-24	-16	< 0.002	4.24	589
L Inferior temporal gyrus	-52	-52	-14	< 0.004	5.18	510
R Inferior frontal gyrus	30	26	-4	< 0.02	4.50	392
R Insula	36	22	4	< 0.02	3.95	
L Superior parietal lobe	-26	-70	42	< 0.02	4.41	355
Regions more active for verbs vs. read						
R Cerebellum	38	-64	-34	< 0.001	7.77	18770
R Lingual gyrus	12	-84	-30	< 0.001	6.77	
L Lingual gyrus	-14	-66	-10	< 0.001	6.46	
L Middle temporal gyrus	-60	-46	-6	< 0.001	5.72	
L Globus Pallidus	-12	-4	4	< 0.001	5.61	
L Cerebellum	-38	-64	-30	< 0.001	5.56	
L Inferior temporal gyrus	-52	-52	-14	< 0.001	5.52	
R Globus Pallidus	12	2	0	< 0.001	4.94	
L Substantia Nigra	-10	-20	-20	< 0.001	4.93	
L Nucleus Caudate	-32	-30	-4	< 0.001	4.87	
L Putamen	-16	8	-2	< 0.001	4.80	
L Cuneus	-4	-100	16	< 0.001	4.73	
R Substantia Nigra	10	-16	-18	< 0.001	4.64	
L Inferior frontal gyrus	-40	6	34	< 0.001	7.31	9454
L Middle frontal gyrus	-6	18	54	< 0.001	6.79	
L Anterior cingulate cortex	-8	24	40	< 0.001	6.34	
R Anterior cingulate cortex	10	26	36	< 0.001	3.79	
R Superior frontal gyrus	8	8	72	< 0.001	3.19	
L Superior parietal lobe	-28	-70	44	< 0.001	5.42	842
L Inferior parietal lobe	-40	-44	36	< 0.001	3.53	
R Inferior frontal gyrus	34	24	-6	< 0.004	4.86	426

Notes: Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $P < 0.05$ corrected, estimated at $p < 0.001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the Voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas and then selecting peaks within each area.

6.3.2.3. High Selection vs. Low Selection

The main aim of the fMRI analyses was to investigate whether selection demands play a role in verb (and/or noun) production, once the potential confound of associative strength is removed. Thus, for each generation task (verb or noun) we compared High versus Low Selection conditions with matched levels of association strength (i.e. (HS-SA) – (LS-SA)). The upper left part of figure 6.4 shows the brain areas that activated during the noun generation task (see also the second contrast of table 6.3). The high minus low selection contrast resulted in the activation of several clusters. The peak activation was in the left postcentral gyrus. In the same cluster the left inferior frontal gyrus, left precentral gyrus, left middle and superior temporal gyri, and some subcortical areas (left putamen, nucleus caudate and pallidum) were also activated. Another large cluster was located in the right hemisphere (precentral gyrus, superior and middle temporal gyri, putamen, insula and claustrum). The upper right part of figure 6.4 shows the regions that activated for the high minus low selection contrast during verb generation (see also the third contrast of table 6.3). In the same way as for noun generation this contrast revealed activation of the left inferior frontal gyrus. As part of a different cluster, the left lingual gyrus and the left cerebellum also showed increased activation for this contrast.

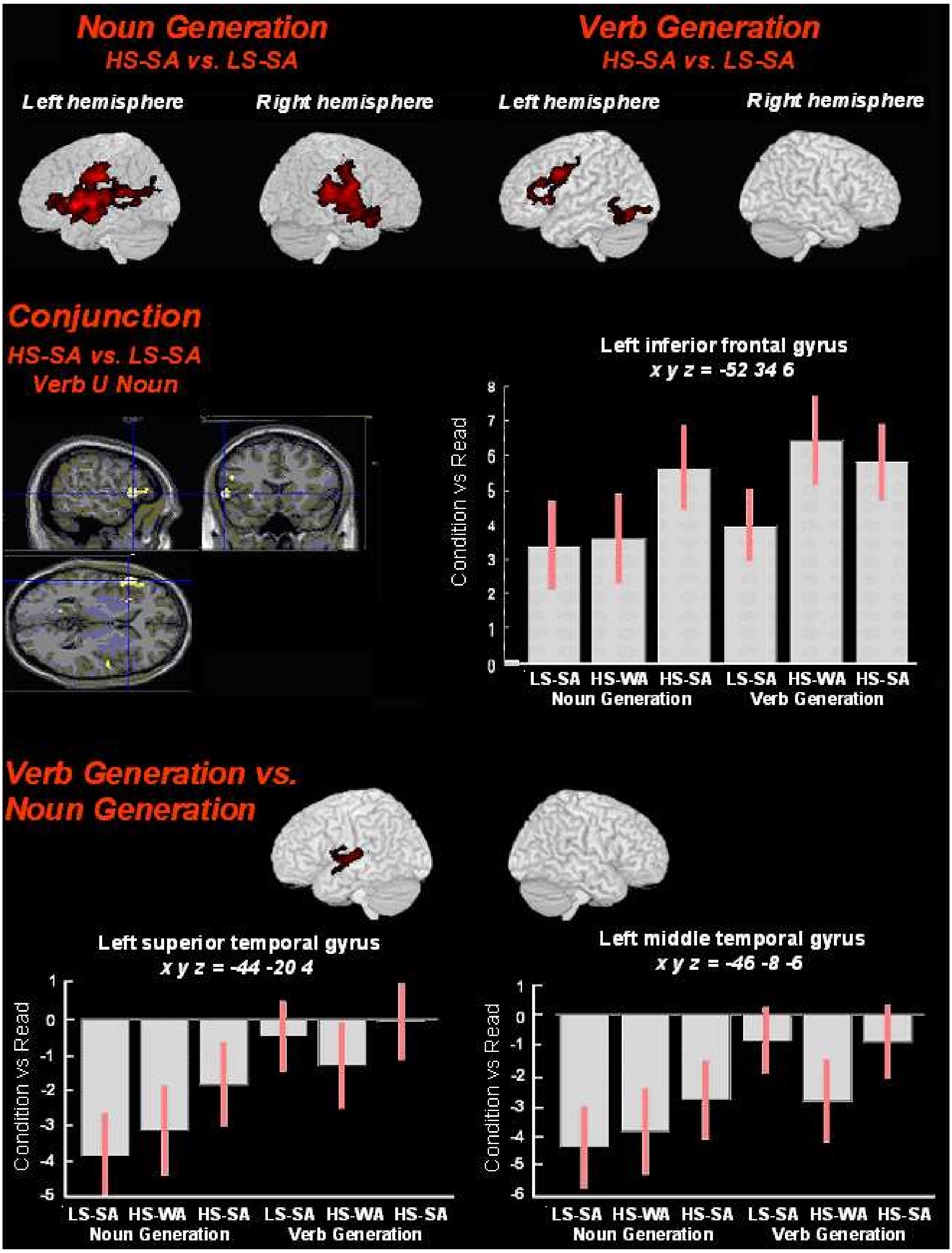


Figure 6.4: Effects of selection demands, conjunction analysis, and Verb vs. Noun contrast. The HS-SA vs. LS-SA contrast is reported for noun and verb generation at the top of the figure (noun generation on the left). The results of the conjunction analysis (HS-SA/LS-SA, Verb/Noun) are reported in the middle of the figure. The results of the contrast Verb vs. Noun are reported at the bottom of the figure. Brain activity in the left inferior frontal gyrus is shown for each condition of the two tasks in the graph in the middle of the figure. Brain activity in the left superior and middle temporal gyri is also reported for the conditions of the two tasks in the graphs at the bottom of the figure. Plots depict activity in experimental conditions relative to the *Read* condition (in arbitrary units [a.u.], +/- 90% confidence interval). LS-SA stands for Low Selection-Strong association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association.

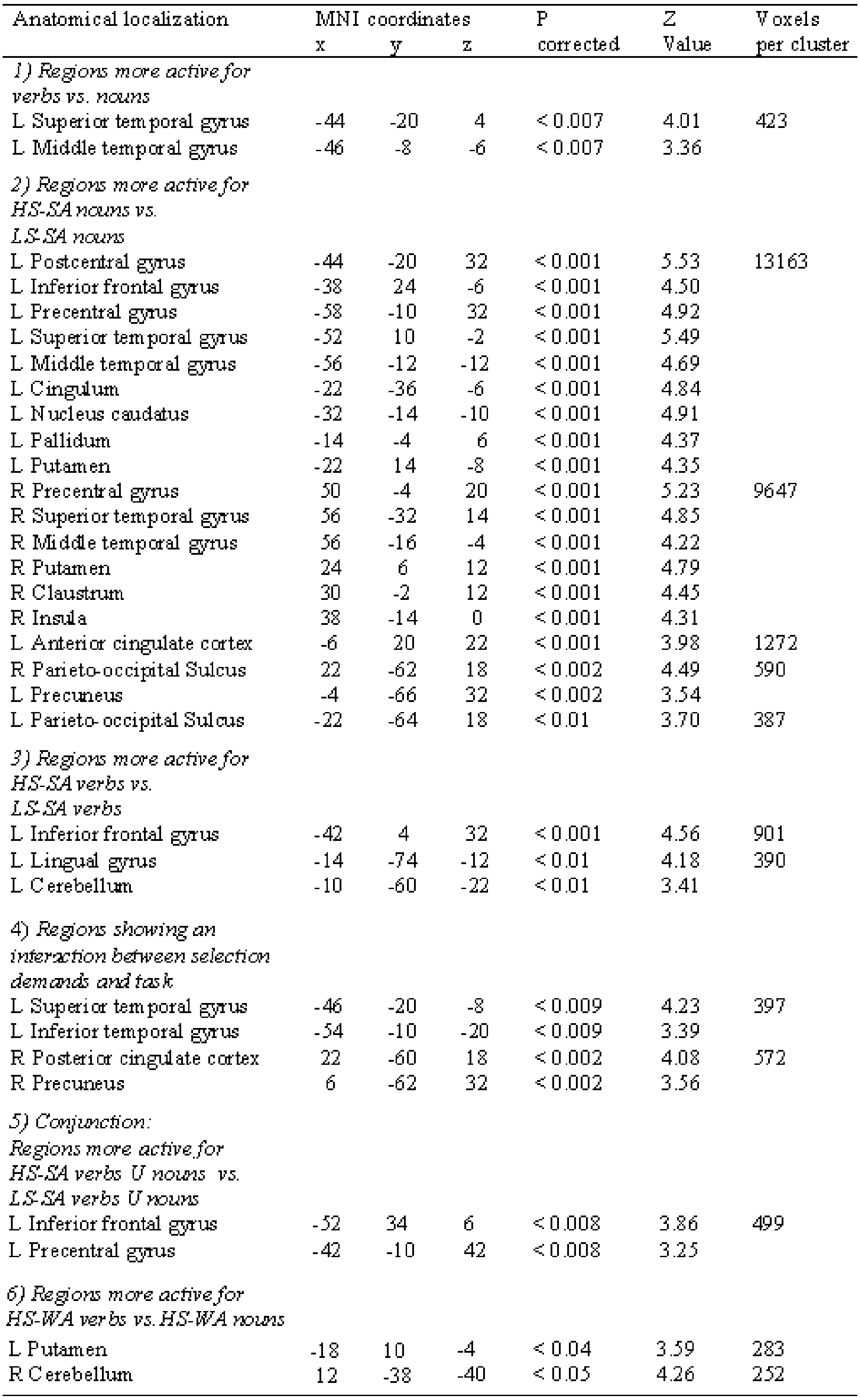
In view of the relatively different patterns of activations (e.g. bilaterally in temporal cortex) which were found between the two tasks for the *HS-SA – LS-SA* contrast, we tested for the interaction between selection demands and task (i.e. HS-SA/LS-SA, Noun/Verb). Two clusters showed a significant interaction (see contrast 4 of table 6.3); the posterior cingulate cortex and the precuneus formed the largest cluster while the left superior and inferior temporal gyri formed a second. The interaction indicates that the decrease in left temporal cortex activation (relative to the read condition) for the nouns relative to the verbs, which gave rise to the *Verb – Noun* main effect, is somewhat reduced for the HS-SA condition of noun generation. In fact in this condition the level of activation of the left temporal cortex was similar for noun and verb generation (e.g. see plots of figure 6.4).

Moreover, since we expected a similar effect of “high vs. low selection” for verb and noun generation we formally assessed this prediction by performing a conjunction analysis (see Nichols, Brett, Andersson, Wager, & Poline, 2005) of (HS-SA) - (LS-SA) for both generation tasks. The middle part of figure 6.4 shows that the only regions that were significantly more active for the HS-SA than LS-SA condition in both tasks were the left inferior frontal gyrus (BA 45) and the left precentral gyrus (BA 6) (see also the fifth contrast of table 6.3).

Finally, we also investigated whether the effects of selection demands which the conjunction analysis showed to be located in the LIFG occur in an area 1) close and functionally similar to that that Badre et al. (2005) reported to be primarily involved in response selection (i.e. left mid-VLPFC, BA 45) 2) but distant and presumably functionally different to the area that these authors reported to be sensitive to manipulation of associative strength (i.e. controlled retrieval, left anterior/ventral VLPFC). To test these hypotheses two sphere ROIs of radius 8mm were extracted using the Marsbar software (http://www.sourceforge.net/projects/marsbar). The peak coordinates of the first ROI were selected referring to the area that was most sensitive to the selection component in the Badre et al.’s (2005) study. Thus this ROI was located in the left mid VLPFC (-54 21 12). In a similar way, the peak coordinates of the second ROI were selected referring to the area that, in Badre et al (2005), was most sensitive to association strength. The second ROI was located in the anterior/ventral VLPFC (-45 27 -15). It should be noted that the cluster of activation found in the main conjunction analysis (HS-SA > LS-SA for both verb and noun generation tasks) was part of the ROI in the mid/posterior VLPFC (-54 18 8), but not of the ROI in the anterior/ventral VLPFC.

As for the whole-brain analyses we compared High versus Low Selection conditions with matched levels of association strength (i.e. (HS-SA) – (LS-SA)) in both tasks and in both ROIs. As far as the verb generation task is concerned, the results confirmed that activation in the mid/posterior VLPFC was significantly higher for HS-SA than LS-SA [t (13) = 3.23, p < 0.001]; while activation in the anterior VLPFC did not differ between these two conditions [t (13) = 1.09, p = 0.14]. In the noun generation task, the HS-SA > LS-SA contrast revealed more activation in the mid/posterior VLPFC [t (13) = 3.83, p < 0.001] but, unlike verb generation, also in the anterior VLPFC [t (13) = 4.88, p < 0.001]. These results show an effect of selection demands focused only in the mid/posterior VLPFC for verb generation, but extending also to the more anterior section of the LIFG in case of noun generation.

Table 6.3. Direct contrasts and conjunction analysis



Anatomical localization	MNI coordinates			P corrected	Z Value	Voxels per cluster
	x	y	z			
1) Regions more active for verbs vs. nouns						
L Superior temporal gyrus	-44	-20	4	< 0.007	4.01	423
L Middle temporal gyrus	-46	-8	-6	< 0.007	3.36	
2) Regions more active for HS-SA nouns vs. LS-SA nouns						
L Postcentral gyrus	-44	-20	32	< 0.001	5.53	13163
L Inferior frontal gyrus	-38	24	-6	< 0.001	4.50	
L Precentral gyrus	-58	-10	32	< 0.001	4.92	
L Superior temporal gyrus	-52	10	-2	< 0.001	5.49	
L Middle temporal gyrus	-56	-12	-12	< 0.001	4.69	
L Cingulum	-22	-36	-6	< 0.001	4.84	
L Nucleus caudatus	-32	-14	-10	< 0.001	4.91	
L Pallidum	-14	-4	6	< 0.001	4.37	
L Putamen	-22	14	-8	< 0.001	4.35	
R Precentral gyrus	50	-4	20	< 0.001	5.23	9647
R Superior temporal gyrus	56	-32	14	< 0.001	4.85	
R Middle temporal gyrus	56	-16	-4	< 0.001	4.22	
R Putamen	24	6	12	< 0.001	4.79	
R Claustrum	30	-2	12	< 0.001	4.45	
R Insula	38	-14	0	< 0.001	4.31	
L Anterior cingulate cortex	-6	20	22	< 0.001	3.98	1272
R Parieto-occipital Sulcus	22	-62	18	< 0.002	4.49	590
L Precuneus	-4	-66	32	< 0.002	3.54	
L Parieto-occipital Sulcus	-22	-64	18	< 0.01	3.70	387
3) Regions more active for HS-SA verbs vs. LS-SA verbs						
L Inferior frontal gyrus	-42	4	32	< 0.001	4.56	901
L Lingual gyrus	-14	-74	-12	< 0.01	4.18	390
L Cerebellum	-10	-60	-22	< 0.01	3.41	
4) *Regions showing an interaction between selection demands and task*						
L Superior temporal gyrus	-46	-20	-8	< 0.009	4.23	397
L Inferior temporal gyrus	-54	-10	-20	< 0.009	3.39	
R Posterior cingulate cortex	22	-60	18	< 0.002	4.08	572
R Precuneus	6	-62	32	< 0.002	3.56	
5) Conjunction: Regions more active for HS-SA verbs U nouns vs. LS-SA verbs U nouns						
L Inferior frontal gyrus	-52	34	6	< 0.008	3.86	499
L Precentral gyrus	-42	-10	42	< 0.008	3.25	
6) Regions more active for HS-WA verbs vs. HS-WA nouns						
L Putamen	-18	10	-4	< 0.04	3.59	283
R Cerebellum	12	-38	-40	< 0.05	4.26	252

Notes: Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $P < 0.05$ corrected, estimated at $p < 0.001$ uncorrected) given in millimeter with effect sizes (*z* scores) and cluster extent. In the Voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas and then selecting peaks within each area. LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association.

6.3.2.4. Effect of weak association

Next, we tested for the effect of association strength that had been found to have a major effect on the behavioural data. Accordingly, we compared in both tasks the high selection-weak association condition with the high selection-strong association one (i.e. (HS-WA) - (HS-SA)). Contrary to the initial prediction this contrast did not reveal any significant activation in either task. However, interesting results were obtained when effects of association strength were investigated within the ROIs extracted in the left mid/posterior VLPFC and left anterior/ventral VLPFC. With regard to the verb generation task, the anterior/ventral VLPFC region was significantly more active for the HS-WA than the HS-SA condition [$t(13) = 1.70$, $p < 0.05$] whereas no differences between these two conditions were found in the mid/posterior VLPFC [$t(13) = 1.31$, $p = 0.1$]. As far as the noun generation task is concerned, neither the anterior/ventral VLPFC nor the mid/posterior VLPFC were more active for HS-WA than HS-SA [$t(13) = -2.05$, $p = 0.97$ and $t(13) = -3.27$, $p = 0.99$ for anterior/ventral and mid/posterior VLPFC ROIs respectively].

These results showed effects of association strength in the left anterior/ventral VLPFC but not in the left mid/posterior VLPFC for verb generation; however no effects of association strength were found in the fMRI data of noun generation.

Finally, an important prediction of our study concerned the HS-WA condition during the two different generation tasks. In particular we asked whether verb and noun generation would differ specifically in the generation of weakly associated items. As reported above (i.e. section 6.1), we expected to find more activity in basal ganglia for verbs than nouns in the weak association condition. For this reason we compared HS-WA verb minus HS-WA noun. Consistent with the prediction, two clusters of activation were identified: one in the left putamen, extending also to the left pallidum, and one in the right cerebellum (see figure 6.5 and contrast 6 of table 6.3). Moreover, in view of these results we tested for the interaction between association strength and task (i.e. HS-WA/HS-SA, Verb/Noun). The left putamen showed a significant interaction ($t = 3.82$, p-corr < 0.05, cluster level, estimated at p-uncorrected threshold < 0.001) while the right cerebellum did not. These results further suggest that the left basal ganglia are particularly activated in the weak association verb condition.

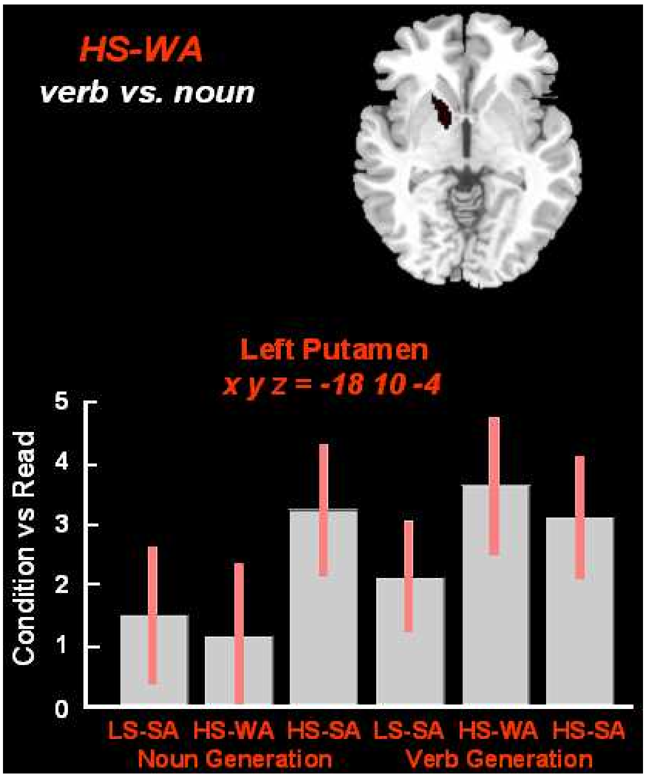


Figure 6.5: Brain areas revealed by the contrast HS-WA verb vs. HS-WA noun. Activity in left putamen is reported in the graph for each condition of the two tasks. Plots depict activity in experimental conditions relative to the *Read* condition (in arbitrary units [a.u.], +/- 90% confidence interval). LS-SA stands for Low Selection-Strong Association; HS-WA stands for High Selection-Weak Association; HS-SA stands for High Selection-Strong Association.

6.4. General discussion

6.4.1. Summary of main findings

The purpose of this study was to provide evidence related to the issue of the competitive vs. associative accounts of verb generation and to investigate the role of the two factors in the activation of frontal-striatal circuits. We used fMRI to address this matter, by extending the classical paradigm of verb production (see Martin & Cheng, 2006) to the generation of nouns (see Chapter 4). Our fMRI results show that the selection between competing responses is an important factor during single word production. The LIFG is more active in situations of high selection than low selection, with association strength matched across conditions. This was the case both for verbs and for nouns as formally shown by the conjunction analysis. More specifically, results of ROI analyses have shown that, for verb generation, effects of selection demands are found in the mid/posterior VLPFC (i.e. ROI in the mid/posterior VLPFC), but not in the anterior/ventral VLPFC (i.e. ROI in the anterior VLPFC) whereas, for noun generation, the ROI analyses showed effects of selection demands in both sections of the LIFG.

The subjects' behaviour on both experimental tasks shows that association strength is also an important factor for both noun and verb production. Weakly stimulus-associated responses require more time and are more prone to errors than strongly stimulus-associated responses. Nevertheless, for both tasks, the condition with weak associations did not lead to any significant activation relative to the condition with strong associations, once selection demands were carefully matched in the two conditions (i.e. the contrast HS-WA - HS-SA). Of importance, the ROI analyses have however shown effects of association strength in verb generation but not in noun generation. Thus, for verb generation the anterior/ventral VLPFC was more active for HS-WA than for HS-SA whereas the mid/posterior VLPFC was equally active for the two conditions.

An important prediction of this study concerned the comparison of the HS-WA condition between the two tasks. Consistent with our hypothesis we found that weakly stimulus-related verbs activated the left BG (left putamen) more than did weakly stimulus-related nouns. Activity in the right cerebellum was also found in this contrast. An interaction between association strength and task was found in the left putamen but not in the right cerebellum. In our previous studies (see chapters 4 and 5), we have argued that the coming to mind of nouns interferes with verb production, but that the complementary situation in noun production generally does not occur. From this perspective, the left putamen could be a key structure involved in coping with the interference that occurs selectively during verb generation.

An unexpected, but noteworthy result concerns the main effect of Verbs vs. Nouns. This revealed greater activation of the left superior and middle temporal gyri for verbs than nouns. In the following sections we provide a possible account for this and the earlier findings referring to the most relevant brain areas for single word generation tasks.

6.4.2. Left inferior frontal gyrus

In this study we replicated and extended the findings of Thompson-Schill et al. (1997; 1998), Barch et al. (2000), and Persson et al. (2004) of LIFG activation following the high vs. low selection comparison. Thus, we provided additional evidence to support the hypothesis that LIFG is important for the selection of information from among competing alternatives. Of importance, a ROI analysis has shown that the left mid/posterior VLPFC rather than the left anterior/ventral VLPFC is involved in this function. This analysis was performed by selecting the areas of the LIFG that Badre et al. (2005) had shown to be primarily involved in response selection (mid/posterior VLPFC, BA 45) and controlled retrieval (anterior/ventral VLPFC, BA 47). The results have shown that, for verb generation, only the mid/posterior section of the left VLPFC was more active for HS-SA than for LS-SA. Nevertheless, effects of selection demands also extended to the anterior left VLPFC for noun generation. Globally these results fit with the finding of our conjunction analysis of HS-SA minus LS-SA carried out for both tasks. Thus, this analysis showed a cluster of activation in a region which partially overlapped with the mid/posterior left VLPFC ROI but not with the anterior/ventral left VLPFC ROI.

Thus, our study sheds further light on the role of the mid/posterior LIFG. Within the domain of semantic knowledge, the selection between alternative nouns or verbs activates this area in a very similar way (see Siri et al., 2008 for LIFG activation related to the production of both action nouns and verbs, and see also Berlingeri et al., 2008, for further evidence on activation of LIFG for both nouns and verbs). Moreover, the fact that in our study the strong association conditions (HS-SA and LS-SA) were carefully matched for the strength and the number of task-irrelevant responses in both tasks fits with the proposal that the mid/posterior LIFG mediates selection of verb and noun responses from among *task-relevant* alternatives.

As shown above, the results of the ROI analyses also showed that the anterior left VLPFC was more active for HS-WA than HS-SA. This effect of association strength was found only for verb generation since the anterior left VLPFC was equally active for the two relevant conditions of noun generation. These results are in line with the behavioural effects of association strength which were much stronger for verb than noun generation (i.e. about 400 ms vs. 100 ms respectively, see section 6.3.1). For the verb generation task the results of the ROI analyses are in line with the functional segregation that Badre et al. (2005) found in the left VLPFC. The anterior/ventral section of this brain region is involved in controlled retrieval from semantic memory whereas the mid/posterior section is more involved in post-retrieval selection in situations of high competition. It is not clear however why the HS-SA condition of noun generation leads to more activation of both sections of the LIFG relative to the LS-SA condition.

A possible reason of why the anterior VLPFC is more active for HS-WA than HS-SA in verb generation only is that in the HS-WA condition of this task, retrieval of task-relevant responses (i.e. verbs) requires the operation of a top-down, control mechanisms. As argued in section 4.5.4 of Chapter 4, such a mechanisms must specify the class of an appropriate response since, as suggested by free association norms (see figure 4.2 in chapter 4), inappropriate responses (i.e. nouns) are frequently spontaneously activated by the stimuli in this condition. As shown in chapter 5 (e.g. section 5.1), Thompson-Schill and Botvinick (2006) have recently proposed a Bayesian framework for verb generation which included a top-down biasing mechanism that adjusts the prior probabilities of response candidates so making the probability of verbs higher than that of nouns during verb generation. The anterior left VLPFC may be a candidate area for the locus of this process. In a similar way, in relation to the FRI model, in chapter 5 we have argued that when no task-relevant response is automatically retrieved in given a condition of the noun/verb generation tasks, more attention is placed on the secondary cue (e.g. "verb" concept), at the expenses of the primary cue (i.e. noun stimulus). This has the effect of binding more tightly the retrieval processes to the desired kind of response. Thus, the left anterior/ventral VLPFC may be important for the attentional modulation of control which is required by the HS-WA verb condition.

Moreover, our study suggests that the activation of the mid/posterior LIFG may not necessarily give rise to behavioural effects such as, for example, an increase of response times for the high selection condition; in fact, the HS-SA and LS-SA conditions of noun generation led to similar RT in our study. A possible explanation for the relatively similar RT in the two conditions with strong association (compared to the situations with weak association) is that in an interactive activation model with positive feedback (e.g. McClelland & Rumelhart, 1981) having two competing alternatives with strong input increases the degree of activation overall, but affects the speed of selection much less than having two competing alternatives with weak input.

As an alternative account, in chapter 5 we have shown that when appropriate parameters of FRI were manipulated, the model was able to show either similar RT on the HS-SA and LS-SA conditions of both tasks (e.g. in the adult subjects' simulation) or longer RT on HS-SA than LS-SA (e.g. in the PD patients' simulation). As already mentioned, an important feature of the ACT-R declarative memory theory is that the probability of generating a given response node is a competitive process which depends primarily on the activation of that specific node but also on the activation of other potential response nodes (see section 5.3.1 of chapter 5). In other words, the strength of the activation of potential response nodes affects the probability to select a given node. As already shown, the activation of a response is positively correlated with the strength of its associative links with the stimulus. Thus differently from the LS-SA condition in which only one response is highly activated, in the HS-SA condition more than one response have high levels of activation. Consequently this latter condition may involve the operation of the mid/posterior LIFG more in the selection of a response from among others with similar probability values. However, in the ACT-R theory, the computation of the RT for a given response node is a non-competitive process that directly reflects the activation level of the selected response. Thus, responses with similar activation values can lead to similar RT in the HS-SA and LS-SA conditions.

Finally, the conjunction analysis also shows that the main area which is activated by the *high selection vs. low selection* contrast in both tasks is BA 45. Robinson et al., (1998; 2005) reported two cases of dynamic aphasic patients (see chapter 2) who had lesions to this brain area. As already shown, both these patients had particular difficulties in the selection of a verbal response when others competed. The authors proposed that this brain area is important in the selection of a response between competing alternatives. Our fMRI study supports this interpretation of these neuropsychological findings.

6.4.3. Basal ganglia

In our study basal ganglia activity was particularly high in the high selection-strong association conditions and also in the high selection-weak association condition of verb generation. Moreover the left putamen also showed an interaction between association strength and task. Recent studies give the basal ganglia a function of inhibiting competing alternatives, and this function is also held to be used in language production (Longworth et al., 2005; Castner et al., 2007; Castner et al., 2008). Indeed, an involvement of basal ganglia structures in lexical-semantic processing has been proposed based on findings both of neuropsychological studies on patients with subcortical lesions (see Copland et al., 2000a; Copland, 2003) and of neuroimaging studies (Rossel et al., 2001; Crosson et al., 2003).

For instance, Rossel et al. (2001) studied the brain correlates of automatic and controlled processing in a semantic priming environment. Automatic and controlled processing were investigated by using short and long prime-target delays. The authors found that the putamen was preferentially activated at long intervals and this led them to suggest a role for this structure in controlled semantic processes. The authors suggested that the putamen may be involved in the processes of response selection and inhibition. A similar conclusion was reached by Copland (2003). He carried out a semantic priming study in which PD patients and controls were presented with auditory prime-target pairs in four different conditions (subordinate meaning unrelated, *bat-river*; dominant meaning unrelated, *foot-money*; subordinate meaning related, *bank-river* and dominant meaning related, *bank-money*) and at two conditions of prime-target interstimulus interval (short and long). Subjects were required to perform lexical decisions to targets (which also included nonwords). The results suggested that PD patients had intact automatic lexical processes, as at short ISI they showed priming in both the dominant and subordinate conditions. However at long ISI, PD patients, unlike normal controls, did not show selective semantic facilitation of the dominant meaning. Copland (2003) argued that this was due to an impairment of inhibitory mechanisms in PD.

Our results are in agreement with the proposed role of basal ganglia in the processes of response selection during lexical retrieval. However we need to consider whether it is appropriate to go a step further by assuming that the activation of the left putamen in the HS-WA condition selectively during verb generation relates to the need to suppress task-irrelevant responses (i.e. nouns) in verb production. This would be consistent with the findings of the PD patients simulation presented in chapter 5. Indeed, we have shown that the manipulation of the inhibition probability (*IP*) parameter, that controlled how frequently the process of response inhibition intervened in FRI, was critical in order to fit the poor performance of the PD patients on the HS-WA condition of verb generation. Of importance, the change in this parameter had much less effect on the ability of the model to produce noun responses in the HS-WA condition of noun generation; this indicates that this condition is less subject to intrusion from task-irrelevant responses (i.e. verb responses) than the corresponding condition of verb generation. Moreover, the finding that young adults are slower with verbs than nouns only in the HS-WA condition (see section 6.3.1) provides further support for the claim that this condition is more prone to interference from non-verb competitors.

An interpretation in terms of inhibitory control exerted by the BG in the HS-WA condition of verb generation also fits with recent evidence for the cognitive role of these structures (Longworth et al., 2005), and with some recent accounts of cognitive deficits of PD patients. For example, in a recent study, Castner et al. (2007) suggest that PD patients have deficits in some aspect of inhibitory control, such as the inhibition of prepotent responses, as well as having problems in selection from competing responses.

Nonetheless, another possibility is to assume that the BG activation in the HS-WA condition reflects the contribution of these structures in accentuating task-relevant information (i.e. verbs in the verb generation task) rather than inhibiting task-irrelevant ones (i.e. nouns in verb generation). Accordingly, as shown in the Introduction of the thesis, it has recently been proposed that the resolution of conflicts between incompatible responses may also occur through a top-down accentuation of task-relevant responses, rather than inhibition of task-irrelevant information (Egner & Hirsch, 2005). In a similar way, McNab and Klingberg (2008) have proposed that PFC and BG operate in concert to filter irrelevant information allowing only relevant information to enter working memory. Moreover, Norman and Shallice, (1986; see also Robbins & Sahakian, 1983) have proposed that BG may operate to potentiate the activation level of schemas in contention scheduling thus biasing their selection in a task-relevant manner. Consistently with this alternative position, in chapter 5 we have also shown that the manipulation of both the *W* and *E* parameters was necessary, too, in order to simulate findings from the PD patients. It should be noted that the ability to differentially activate task-relevant information relative to non-relevant information was manipulated in FRI by varying *W* (see also Daily et al., 2001) while large values of *E* caused reduced energization, that is, a slower activation of the relevant responses in successive retrieval attempts in our model.

It is important to note that the two possibilities briefly reported above (i.e. inhibition of task-irrelevant responses and accentuation and selection of task-relevant ones) may not be mutually exclusive; in fact recent evidence has shown that response selection and response inhibition may involve similar mechanisms both relying on the operations of fronto-striatal circuits (Mostofsky & Simmonds, 2008); our FRI model also suggests that both abilities are needed in verb generation, particularly in situations of weak association (i.e. HS-WA) and that they can both depend on the operations of PFC and BG.

There is also a third possibility for why the basal ganglia are more active for verbs than nouns in the HS-WA condition. This is related to the way that verb retrieval may depend on the efficiency of the representation of actions (e.g. Silveri & Misciagna, 2000). According to this view, the basal ganglia could be involved in verb processing because of their well known function in motor control (Mink, 1996) and through its functional links with the frontal lobe. For example, Signorini and Volpato (2006) found that PD patients were impaired on an action fluency task but not on semantic and letter fluency tasks.

6.4.4. Left temporal lobe

We found that verb generation activated the left superior and middle temporal gyri more than noun generation (see the first contrast of table 6.3). The generation of nouns semantically related to noun stimuli has not been widely studied yet. An exception is the PET study of Warburton et al. (1996). These authors studied noun and verb retrieval in normal subjects. Noun and verb generation tasks were also contrasted with a rest control condition. Similar to here, Warburton et al. found that both tasks compared to rest activated the same regions in the superior temporal gyrus (bilaterally), left inferior frontal gyrus, anterior cingulate cortex, supplementary motor areas (SMA) plus several subcortical areas. Moreover, the direct contrast of verb minus noun generation revealed activation of the left inferior temporal gyrus (as well as the left inferior parietal lobe, LIFG and SMA). Warburton and colleagues suggested that the inferior temporal gyrus and the posterior part of the inferior parietal lobe are important in lexical processing and in particular in the access to semantic fields (see also Yokoyama et al., 2006, for further evidence showing that activation of the left middle temporal gyrus is increased for verbs relative to nouns).

One possibility related to that put forward by Warburton et al. (1996), is that semantic priming effects may be stronger for noun than verb generation. Recent neuroimaging studies have shown decreased activation in several brain areas in conditions of repetition priming, including regions of the temporal lobe (for a review see Schacter & Buckner, 1998; and Henson, Shallice, Josephs, & Dolan, 2002). In an fMRI study of implicit semantic priming, Rissman et al. (2003) studied the brain correlates of a lexical decision task in the context of prime-targets pairs. The targets could be semantically related or unrelated to the prime or they could be nonwords. The authors found decreased activation in the left superior temporal gyrus (as well as in the left precentral gyrus, left and right middle temporal gyri and right caudate) when the related targets condition was compared to the unrelated condition (see also Copland et al., 2003, for similar findings of neural priming in left middle temporal gyrus in a lexical decision task). The authors argued that this finding could be due to the enhanced neural efficiency occurring in the recognition of related targets.

We propose that, in our study, noun stimuli elicit many other nouns with related semantic features; this would have the effect of reducing the left temporal gyrus activation in situations of noun generation (see below). By contrast, during verb production subjects have to explicitly attend to the semantic relationship between the stimulus and response (see Martin & Byrne, 2006; and Thompson-Schill & Botvinick, 2006). In agreement with this, previous analyses of free association responses using the same stimuli as in the current fMRI experiment (see the task-relevant response analysis of chapter 4) showed that nouns are spontaneously produced much more often than verbs in response to noun cues.

However, there is a difficulty for an interpretation in terms of semantic priming of the increased activation in the left temporal lobe for verbs relative to nouns. In situations of strong association, the generation of verbs is actually faster than noun generation (see figure 6.2). In chapter 5 we have proposed that verbs can be produced faster than nouns because the associative strength between the concept “noun” and all its related noun responses is weaker than the associative strength between the concept “verb” and all its associated verb responses. This is simply due to verbs being less numerous than nouns and to the fact that, in ACT-R, the “fan” of activation spreading from cues to each related node decreases as the number of associates increases. Thus, in verb generation the concept “verb” would spread more activation to verb responses than would do the concept “noun” to noun responses. In their model (see chapter 5), Martin and Byrne (2006) have proposed that the automatic search through semantic memory (i.e. in situations of strong stimulus-response association strength) through a spread of activation may depend on processes carried out in left temporal regions. The present results confirm that the potential difference in the degree of activation spreading between noun and verb generation may give rise to more activation in the left temporal lobe for verbs than nouns.

Finally, as reported above, the main effect of *verb – noun* suggests that globally noun generation leads to less activation of the left temporal lobe than does verb generation. However the results of the interaction between *selection demands* and *task* indicate that the *HS-SA vs. LS-SA* contrast activates the superior and inferior parts of the left temporal cortex more for noun than verb generation. A possible explanation for this difference could be that in the HS-SA condition of noun generation more than two strongly associated items are activated; thus activation spreading would be increased in this situation relative to the LS-SA condition.

6.5. Conclusions

We investigated the role of selection and association during verb and noun generation. For both types of task, we found that the mid part of the left inferior frontal gyrus was more active in conditions requiring high compared to low selection, highlighting the central role of this region in mediating the selection between competing responses. This was also suggested by a ROI analysis. Association strength influenced behavioural performance, but did not produce any specific brain activation following a whole-brain analysis. However, when a ROI was extracted in the anterior/ventral region of the VLPFC (BA 47) an effect of association strength was found for the verb generation task but not for the noun generation task. These results suggest that controlled retrieval is subserved by this brain region and that it is more needed during verb than noun generation. Moreover, we found that the basal ganglia and the cerebellum were more active when weakly associated verbs had to be produced relative to weakly associated nouns. An interaction between association strength and task was found in the former but not in the latter structures. This suggests that association strength becomes critical when task-irrelevant stimuli interfere with the current task (here nouns during verb production), triggering additional activation of the basal ganglia. We conclude that both the selection between competing responses and association strength are important factors for single word production with association strength becoming critical only in the verb generation task and particularly when task-irrelevant responses interfere with word production.

These findings are in line with our previous results obtained on both PD patients, who had the greatest difficulties in producing weakly stimulus-related verb responses, and by running simulations on the FRI model.

Chapter 7

7.1. Summary and discussion of the current project

As described in the first chapter, researchers working in cognitive neuroscience try to uncover and identify the elementary cognitive processes that contribute to overt behaviour; nonetheless they are also interested in discovering the neural mechanisms that underlie these processes. Cognitive neuroscientists typically make use of different methodologies and approaches to understand the neural basis of human cognitive functions and the constant interaction between the cognitive level and the neural level of investigation is critical for the progress of this scientific subject (e.g. Shallice, 1988; Gazzaniga et al., 2002).

The present project started from the purpose of investigating the role of the prefrontal cortex (PFC) and basal ganglia (BG) in the selection of task-relevant information. To this end, a multi-disciplinary approach has been used. As reported in the previous chapters, different methodologies have complemented each other and have contributed to better specify the processes underlying different tasks in the domain of the higher levels of the language production system.

In this chapter, the results of the project will be discussed. In particular we will explain how these results contribute to the understanding of both the processes underlying the performance of different cognitive tasks and of the role that PFC and BG may play in these processes. Thus, in the following paragraphs, the main results of the project will be reviewed. We will start from the findings obtained on normal adult subjects on tasks of sentence and stem completion (i.e. second part of chapter 2); we will then discuss the results of the neuropsychological studies, first that on patient OTM (i.e. chapter 2) and second that on PD patients (i.e. chapter 4). Subsequently, the results of the computational models will be reviewed; first, we will discuss the results of the COGENT macroplanning model (i.e. chapter 3) and second, we will review the findings obtained on the FRI model (i.e. chapter 5). Moreover, the results of the fMRI study (i.e. chapter 6) we will be reviewed and discussed. Finally, the last section of this chapter will deal with the general implications of the overall project and some suggestions for future research will be discussed.

Selecting responses from among alternatives in normal adult subjects

The first aim of this project was to characterize the processes and to reveal the brain areas underlying the ability to select verbal responses in situation of high competition. In the domain of language, there is broad consensus that our ability to respond to situations which afford multiple possible responses relies on left prefrontal cortical regions (Nathaniel-James & Frith, 2002; Persson et al., 2004; Thompson-Schill et al., 1997; 1998). In the second part of chapter 2 we have reported two behavioural studies which aimed to investigate the ability to select responses from among alternative options in normal adult subjects. In a first experiment, subjects were asked to complete sentences either through single words or entire phrases and 3-letter stems with single words. Each of the three tasks involved both stimuli with high selection demands (i.e. low response predictability sentences and stems with *many* possible completions) and stimuli with low selection demands (i.e. high response predictability sentences and stems with *few* possible completions). We have shown that low response predictability sentences are slower to be completed than high response predictability ones both by mean of single words and entire phrases. These results are in line with those of certain neuropsychological studies in which dynamic aphasic patients were administered similar tasks of sentence completion (see Robinson et al., 1998; Robinson et al., 2005; see also chapter 2). The results fit also with those of other neuropsychological and fMRI studies which reported longer RT for stimuli with high relative to low selection demands in the context of verb generation experiments (see Thompson-Schill et al., 1997; 1998; Persson et al., 2004; see also chapter 4 and below in this chapter). As far as the stem completion task is concerned, the results have shown that stems with *many* and *few* possible completions lead to similar RT. Critically, in our study the words which acted as completions in the *many* stem condition were matched for frequency of occurrence to the words which acted as completions in the *few* stem condition. This was done because of the hypothesis that word frequency, more than selection demands, was the crucial factor influencing performance in the stem completion task (see Ryan et al., 2001).

In a second study we employed a dual task paradigm in which subjects were asked to carry out the same three language tasks while at the same time performing a distracting motor task at two conditions: less demanding and more demanding. The straightforward prediction was made that the more demanding version of the motor task would specifically influence performance (i.e. increased RT) on the low response predictability sentences but not on the condition of the stem completion task with high selection demands (i.e. the *many* condition). Accordingly, the results have shown that RT specifically increased when subjects had to produce single words or phrases in order to complete low response predictability sentences while simultaneously performing the more demanding version of the motor task. This was not the case for the stem completion task in which analogous RTs were found for both the *many* and the *few* conditions irrespective of the motor task.

As shown in chapter 2, the type of distracting motor task that we used has been reported as affecting performance of some tasks which require PFC (Moscovitch, 1994; Fletcher et al., 1998). In particular, in a PET study of episodic memory Fletcher et al. (1998) have shown that the distracting motor task reduced activity over the left PFC particularly in the conditions in which subjects were required to organize word lists semantically, namely when executive control was needed in order to create an organizational structure at encoding. Accordingly, we have proposed that low response predictability sentences rely more on the operations of the left PFC than high response predictability sentences because the former require more processing demands than the latter. The enhanced processing demands would be due to the need to select a response from among others in competition. On the other hand, we suggested that the analogous RTs required by the *many* and the *few* stems as well as the fact that the more demanding version of the dual-task does not influence the performance on the *many* stems, indicate that both the two conditions of the stem completion task require similar processing demands despite the differences in selection demands. Thus, we have argued that bottom-up activation of the target representations (i.e. high frequency completions) was sufficient to result in recovery of the relevant responses in both conditions of the stem completion task. In other words, selection of task-relevant information may occur in a more automatic way in the stem completion task than in the sentence completion task as far as the low response predictability sentences are concerned.

Response retrieval and selection in dynamic aphasia and in Parkinson's disease

As shown in chapter 2 (see sections 2.1 and 2.1.1) the ability to select responses in situations of high competition may be dramatically disrupted after brain damage involving the left PFC. The investigation of patients with dynamic aphasia also suggests that the left frontal lobe, and in particular its inferior part (i.e. left inferior frontal gyrus, LIFG), is important for response selection in situations of high competition (Robinson et al., 1998; Robinson et al., 2005). From another perspective, neuroimaging studies, too, have shown that the LIFG plays an important role in the process of selection of responses between competing alternatives (e.g. Thompson-Schill et al., 1997; Persson et al., 2004).

In chapter 2 we reported the results of a study carried out on a patient, OTM, who was unable to complete low-response predictability sentences (i.e. with high competition in the response set), either through single words or phrases, despite performing in the normal range with high-response predictability sentences (i.e. with low competition in the response set). OTM also had more problems in producing sentences when word pairs were weakly rather than strongly associated, or when he was asked to create sentences from, but not to simply describe, single pictures (see table 2.4 in chapter 2 for all verbal generation tests). More generally, OTM's language production was characterized by reduced fluency particularly in situations requiring more than a simple description of the stimulus. His language output deficit was not accompanied, however, by reading, repetition, naming, and comprehension deficits as these skills were either preserved or only mildly impaired. This pattern of deficits was consistent with dynamic aphasia (Luria, 1973); indeed we showed that OTM' speech-rate was much lower than that of normal controls but similar to that found in other dynamic aphasic patients (see table 2.3 in chapter 2).

It should be noted that OTM did not suffer from a lesion to the left frontal regions but to the BG. Previous studies which reported cases of dynamic aphasia after lesions to the BG (e.g. Raymer et al., 2002; Gold et al., 1997; Robinson et al., 2006) have consistently shown that BG lesions which cause dynamic aphasia also lead to deficits in extra-language cognitive processes. As discussed in the second chapter (see sections 2.1. and 2.7), Robinson et al. (2006) have proposed a distinction between two subtypes of dynamic aphasia arguing that their patient (KAS) suffered from the second subtype since, following lesions involving bilateral frontal and subcortical structures, she had verbal and non-verbal generation deficits and problems with discourse level generation tests. According to Robinson et al. (2006), KAS was defective in the generation of a fluent sequence of novel thoughts possibly because of a deficit in focusing attention.

In our study we tested whether OTM too had deficits in domains other than language. A series of non-verbal generation tasks showed that OTM had problems both in generating numbers randomly in a random number generation task and novel figures in a figural fluency test. These findings were interpreted as due to a deficit of either inhibition or novel content generation for OTM. A potential failure of inhibition or of novel content generation was also in line with the perseverative behaviour that our patients showed in some language tasks, such as generation of sentence from common words and proper nouns and, more generally, with his problems in selecting a response between alternative options. Thus, we proposed that patient OTM suffered from an impairment in novel thought generation that, within the domain of language, was particularly manifest in situations of high competition, namely when a response was to be selected between others in competition.

More generally the findings on patient OTM confirm Robinson et al.'s (2006) proposal that sub-varieties of dynamic aphasia exist and further suggest that the potential role of BG in the suppression of competing alternatives and, more generally, in response selection may not be specific to language extending instead to different cognitive domains (e.g. Redgrave et al., 1999; Longworth et al., 2005; Crosson et al., 2007).

In a following neuropsychological study we have further investigated the role of fronto-striatal circuits in selection of task-relevant verbal information. To this end we used a paradigm of noun and verb production that allowed us to dissociate the contribution that different factors (i.e. selection of responses from among alternative options and strength of stimulus-response association) provide to single word production. We used PD patients as a model of impairment of BG function (e.g. Ullman et al., 1997; Copland, 2003). Previous studies (e.g. Péran et al., 2003) have accounted for the findings of impaired verb but not noun generation in PD patients in the light of the signs of frontal dysfunction that these patients generally show. The rationale behind this explanation is simple and is that the grammatical category of verbs would activate frontal regions more than nouns (e.g. Shapiro et al., 2006).

In our study we have used the verb generation paradigm of Martin and Cheng (2006), extending it to noun generation as well. As shown in chapter 1 (see section 1.3) and chapter 4 (see section 4.1) currently there is a debate on verb generation. The core of the dispute focuses on whether selection between alternative verb responses (Thompson-Schill et al., 1997; Thompson-Schill & Botvinick, 2006) or strength of stimulus-response associative links (Martin & Cheng, 2006; Martin & Byrne, 2006) is the critical factor influencing performance on the verb generation task. The paradigm of Martin and Cheng (2006) gave us the possibility to investigate whether the potential problems of PD patients with verbs are uniformly present for this grammatical category or depend on factors such as stimulus-response associative strength and selection between multiple responses.

Our results have shown that both factors of response selection and associative strength influence single word production with the latter factor having a greater impact on performance than the former. Indeed both subject groups performed the weak association condition of the verb generation task worse (lower accuracy and slower RT) than the strong association conditions. On the other hand, an effect of selection demands (high selection performed poorer than low selection) was only found in the verb generation task, and it was greater for PD patients than older controls. The most striking finding of our study was the extremely poor performance of PD patients in the condition of verb generation in which weakly-stimulus related verb responses were to be produced. The patients often produced nouns instead of the verbs that were required in this condition. Importantly, additional analyses (e.g. Task-Relevant response, see sections 4.3.3 and 4.4.5 of chapter 4) have suggested that the generation of task-irrelevant responses by subjects have different consequences for the performance of the two tasks. In particular inappropriate noun responses interfere during verb generation more than verb responses do during noun generation. In more detail, the findings indicate that noun responses interfere particularly during the weak association condition of verb generation.

Accordingly, we have suggested that PD patients are less able to access task-relevant responses in the context of both weak stimulus-responses association strength and highly activated task-irrelevant competitors and also that they are impaired in the selection of responses from among retrieved task-relevant competitors. More generally, the data have suggested that the BG may be important in both the two processes involved in the “two-process model of fronto-temporal control of semantic memory” of Badre et al. (2005), namely the processes of controlled (associative) retrieval and selection during retrieval.

Moreover, the finding of strong correlations between PD patients’ performance on verb generation and their scores on frontal executive tests also suggests that their poor verb generation performance was not due to an isolated grammatical deficits as suggested by others (Ullman et al., 1997; Grossman et al., 1994) but reflected more general deficits in the supervisory functions of semantically controlled retrieval and selection of responses from among competing options.

The results of this study have confirmed the findings on patient OTM and have further suggested that the BG and more generally frontostrital circuits contribute to the process of selection of task-relevant verbal responses by mean of functions which may not be specific to the language domain.

Computational models of tasks performance

As shown in previous chapters, in this project a range of different methodologies and approaches have complemented each other and have provided cumulative evidence in favour of the hypothesis that frontostriatal circuits play a critical role in the process of selection of task-relevant responses. In particular, in chapters 3 and 5 we have proposed two detailed functional models of task performance. Two different kinds of model were chosen. The model presented in chapter 3 was based on the COGENT information processing package (Cooper,

2002) and addressed the issue of how different sub-processes operating at the level of the conceptual preparation of language interact during the creation of preverbal messages. The model presented in chapter 5 (i.e. the FRI model) was based on the declarative memory system of the ACT–R theory (Anderson et al., 2004) and it was complemented by general theories of executive control (e.g. Stuss et al., 2005). The declarative memory module of ACT-R concerns the activation processes that control access to information in declarative memory and its behavior is controlled by a set of equations and parameters (see section 5.3.1 in chapter 5). The FRI model focused on the tasks of noun and verb generation which were administered to young adults (chapter 5), older subjects and PD subjects (chapter 4).

Generally speaking both the COGENT and the ACT-R framework can be considered as hybrid systems as they support models which combine both symbolic and subsymbolic approaches. Thus, as shown in chapter 1, the COGENT cognitive modelling environment involves both rule-based and connectionist simulations (see chapter 3 and appendix 1 for examples of rule-based processes). In a similar fashion, at the core of ACT-R there is an activation-based production system consisting of a production system component (see chapter 1) augmented with a learning mechanism and perceptual and motor systems. A distinctive feature of ACT-R is given by its subsymbolic component. In fact, elements in working memory have activation levels which influence their probability of being selected. An important difference between the COGENT information-package and the ACT-R cognitive architecture is that the first accommodates many different theoretical frameworks, that is it does not embody any particular theory of the cognitive architecture, while the second is a detailed theory of the large-scale structure and organization of cognitive processing which aims to provide a unified framework within which models of specific tasks can be developed.

As shown above and in chapter 3, our first model focused on the macroplanning processes which are required in order to perform the sentence completion task. As already discussed (see section 3.1 in chapter 3), previous models of language production specified the processing stages involved in lexical and phonological encoding much better than those occurring at the level of conceptual preparation (e.g. Roelofs, 1992; 1997). In chapter 3 we have tried to provide a better specification of the higher-levels of the language production system by embedding our macroplanning model in the DOMINO framework (Fox & Das, 2000). This was done because this framework deals with planning/executive processes, such as setting of high-level goals, strategy generation, problem solving, and implementation and selection of plans and actions, which are also required during the encoding and selection of messages which act as candidate sentence completions (e.g. generation of communicative intentions and selection of information for expression). Moreover, the facts that the DOMINO framework has been used to model some aspects of the SAS system (Glasspool, 2000), also in a COGENT implementation (see the WCST model of Cooper, 2002) and that macroplanning has not been yet addressed by the ACT-R theory, motivated the choice of using COGENT for our macroplanning model.

As far the FRI model is concerned, in chapter 5 we have shown that this model is compatible with existing functional models of verb generation (i.e. Thompson-Schill & Botvinick, 2006; Martin & Byrne, 2006). Thus, both the Bayesian framework of Thompson-Schill and Botvinick, (2006) and the model of Martin and Byrne (2006) relied on the strength of stimulus-response associations (see section 5.1 in chapter 5). In both these models response selection is determined by the conjoint activation from multiple retrieval cues (e.g. see figure 5.2 in chapter 5; see also primary and secondary in our model; i.e. figure 5.4 in chapter 5) which trigger a spread of activation across a set of potential responses. As shown above, a set of equations and parameters within the declarative memory module of ACT-R controls how information is accessed in declarative memory (see Anderson et al., 2004; see also Danker et al., 2008). The pertinence of Thompson-Schill and Botvinick, and Martin and Byrne's models to the ACT-R memory theory motivated the choice of using this set of equations in our FRI model. Moreover, in chapter 5 (see section 5.1) we have shown that both the two previous models made specific assumptions about the executive control operations which are required by verb generation (e.g. strategic allocation of attention on multiple retrieval cues, response override). In the FRI model we have implemented these operations as separate LISP functions.

Turning to the findings obtained on both models, in chapter 3 we have shown that the COGENT model involved a simulation of the sentence completion task which aimed to reproduce the performance that both OTM and normal adult subjects showed on this task. The model concerned both a symbolic formalism, expressed in terms of production rules, and an approach in terms of connectionist, parallel processes. The COGENT model aimed to test a specific hypothesis about the verbal output deficit of patients with dynamic aphasia, namely that this disorder is due to an impairment in creating and selecting preverbal messages specifically in situations of high competition (Robinson et al., 2005; Robinson et al., 1998; see also sections 2.1 and 2.1.1 in chapter 2).

The results of the simulation have provided evidence that OTM's poor generation performance in the low response predictability sentences may occur because of an abnormally balance between the values of a self activation and a lateral inhibition parameters of an interactive activation network (IAN). We have argued that these findings fit with the suggestion that the BG are important for selecting responses in situation of high competition in a contention scheduling framework (Norman & Shallice, 1986) and more generally with the suggestion that fronto-striatal circuits may operate to filter task-irrelevant information in order to allow selection of task-relevant responses (e.g. McNab & Klingberg, 2008).

In general terms, the findings obtained on both OTM and the COGENT model have contributed to strengthen the view that the relation between cognitive modelling and cognitive neuropsychology can be bidirectional (see section1.1 in chapter 1). Indeed, on the one hand the latter informs the former by providing data against which models can be tested while, on the other hand, cognitive modelling may be a supplement to cognitive neuropsychology since it helps explaining in more detail the deficits observed in the patients.

With regard to the FRI model, we have shown that it was based on the functional interaction between aspects of selection of responses and stimulus-response associative strength. The model assumed that noun/verb generation requires three processing stages: (1) allocation of attention on retrieval cues (*F*ocusing) (see figure 5.4 in chapter 5), (2) associative retrieval (*R*etrieve), and (3) response inhibition (*I*nhibit). We have also assumed that recovering from a retrieval failure and initiating a new retrieval attempt require time and executive resources (i.e. *E* –energization). In the FRI model a stimulus triggers an initial spread of activation over a series of candidate response nodes. A series of equations derived from the ACT-R theory (see section 5.3.1) aim to retrieve and select one of these response nodes; finally the selected response nodes are checked and eventually inhibited in the model. In the situations in which a response node is inhibited a second retrieval attempt is initiated in the FRI model; more attentional resources are allocated to the secondary cue (i.e. the concept "verb" in verb generation, see figure 5.4 in chapter 5) and this has the effect to bias retrieval toward task-relevant responses in these circumstances.

A simulation was run in order to make the FRI model reproduces the performance of young adults, older adults, and PD patients on the noun and verb generation tasks. The manipulation of only three parameters, which referred to the executive processes involved in the model, namely *W* (attentional resources available for retrieval); *IP* (probability that response checking and inhibition are triggered); and *E* (energization), allowed the FRI model to fit the data of all three subject populations. Of particular importance are the results of the simulation of PD patients. The poor verb generation performance of these patients required the manipulation of all three parameters. In line with our previous interpretation of their deficits, the FRI model has suggested that PD patients have difficulty in copying with highly active task-irrelevant responses; moreover simulation results have also suggested that they are much slower than normal controls in initiating re-allocation of their reduced attentional resources.

More generally, the FRI model has shown that the debate on verb generation between the positions of response selection/competition (Thompson-Schill et al., 1997; 1998; Thompson-Schill & Botvinick, 2006) vs. associative strength (Martin & Cheng, 2006; Martin & Byrne, 2006) can be reframed to propose that they can be integrated into a unitary model. The competition factor may reflect specific dynamic of response selection at a relatively early stage of verb/noun generation (e.g. ACT-R memory system). On the other hand, effects of associative strength are particularly evident in the weak association condition of verb generation and are likely due to the interference caused by task-irrelevant competitors.

Finally the FRI model, like the COGENT model, has also suggested that the BG have an important role in the processes of response selection and inhibition as well as in energizing schemata and, more generally, has indicated that fronto-striatal circuits are important for allocating attentional resources strategically in order to bias retrieval in a task-relevant manner.

Brain correlates of selection of task-relevant responses

In a following study we used functional brain imaging to explore the brain correlates of the process of selection of task-relevant responses. More specifically, in an fMRI study based on the same paradigm of noun and verb generation we have tried to dissociate response selection and association strength and to investigate the role of these two factors in the activation of fronto-striatal circuits.

Effects of response selection were expected to occur in the mid and posterior part of the LIFG (e.g. Badre et al., 2005; Thompson-Schill, et al., 1997; Persson et al., 2004) while effects of association strength were expected to be found in the more anterior/ventral section of the LIFG (Badre et al., 2005) and, following our study on PD patients (see chapter 4), in the BG specifically when the weak association condition of the verb generation task was compared to the corresponding condition of noun generation.

Our fMRI results have shown that the mid LIFG is more active in situations of high selection than low selection, with association strength matched across conditions (i.e. HS-SA > LS-SA). This was the case both for verbs and for nouns. Thus, our study has extended existing findings on verb generation (Thompson-Schill et al., 1997; Persson et al., 2004) to noun generation for the first time and has also confirmed that selection between competing responses is an important factor for single word generation. Following the functional segregation within the LIFG proposed by Badre et al. (2005), we also carried out ROI analyses in both the left mid/posterior VLPFC (response selection, Badre et al., 2005) and left anterior/ventral VLPFC (controlled retrieval, Badre et al., 2005; see sections 6.3.2.3 and 6.3.2.4 in chapter 6). As far as the factor of selection demands is concerned the results showed significant effects (i.e. HS-SA > LS-SA) focused only in the mid/posterior VLPFC for verb generation, but extending also to the more anterior section of the LIFG in case of noun generation.

With regard to the effects of association strength we obtained that, following a whole-brain analysis, they were not found in any brain regions. In fact, for both tasks, the condition with weak association did not lead to any significant activation relative to the condition with strong association (i.e. HS-WA = HS-SA). However the ROI analyses have shown effects of association strength in verb generation but not in noun generation. Thus, for verb generation the anterior/ventral VLPFC was more active for HS-WA than for HS-SA whereas the mid/posterior VLPFC was equally active for the two conditions. For the verb generation task the results of the ROI analyses fit with the functional segregation put forward by Badre et al. (2005) for the left VLPFC. The anterior/ventral section of this brain region is involved in controlled retrieval from semantic memory whereas the mid/posterior section is more involved in response selection in situations of high competition. In chapter 6 (see section 6.4.2) we also proposed that the effects of association strength were specific to verb generation because of the fact that especially in the HS-WA condition of this task a top-down, control mechanism is required in order to retrieve task-relevant responses. This position was argued to be compatible with the findings obtained on both PD patients (see section 4.5.4 in chapter 4) and the FRI model (i.e. attentional modulation of control particularly needed in the HS-WA verb condition; see section 5.5 in chapter 5).

Moreover, when the conditions with weak association of the two tasks were compared, activity in the left BG was found to be increased for verbs relative to nouns. An interaction between association strength and task was also found in the left putamen. In line with our previous interpretation of BG cognitive function, we interpreted the activation specific to the weak association condition as due to the need to either suppress task-irrelevant responses in verb generation (i.e. noun responses) or accentuate task-relevant responses in this task (i.e. verbs in verb generation). These proposals are in line with the results obtained on the FRI model (see subsection above). In fact we found that the model was able to fit PD patients data only when we reduced both the abilities to inhibit irrelevant responses (i.e. decrease of the IP parameter in the FRI model), and to accentuate relevant responses (i.e. increase of E and decrease of W parameters).

An aspect of the fMRI study which deserves further consideration is related to the effects of selection demands which we found to be small from a behavioural point of view but large from the point of view of the fMRI data. In chapter 6 we referred to the FRI model in order to account for such a divergence between imaging and behavioural data. Thus, in chapter 5 (see section 5.3.1, equations 4 and 5) we have shown that, following the ACT-R theory, the probability of generating a given response node in the model is a competitive process which depends on both the activation of that specific node and on the activation of other potential response nodes. Thus, the strength of the activation of potential response nodes affects the probability to select a given response node. Moreover, we also showed that in ACT-R the activation of a response is positively correlated with the strength of its associative links with the stimulus; in other words, the stronger the associative strength between a stimulus and a response node the more active is this response node. Thus, in our task paradigm and in the FRI model, stimuli with high selection and strong association strongly activate more than one response node unlike stimuli with low selection demands which strongly activate only one response. Consequently, we have proposed that (see section 6.5 in chapter 6) the condition with high selection demands may involve more the operation of the LIFG of selection of a response from among others which have similar probabilities to be selected.

Another important feature of the ACT-R theory is that, however, the computation of the RT for a given response node is a non-competitive process that directly reflects the activation level of the selected response. Thus, responses with similar activation values (i.e. similar association strength) can lead to similar RT in the conditions which differ in selection demands but not in association strength.

Another aspect of our fMRI study deserves more attention. This is related to the finding of more activation in the left superior and middle temporal gyri for verbs than nouns. In the discussion section of chapter 6 (section 6.4.4) we proposed two possible explanations for this result. The first is based on mechanisms of semantic priming which would be stronger for nouns than verbs so resulting in less activation in the temporal cortex for the former than the latter. The second explanation is again based to the findings obtained on the FRI model. The fact that verbs are less numerous than nouns in the language and in the semantic network used in the FRI model, caused the associative strength between the secondary cues and their associated response nodes to be weaker for nouns than verbs (see figure 5.4 in chapter 5). Previous studies (e.g. Martin & Byrne, 2006) have proposed that the automatic search through semantic memory may depend on the left temporal regions. Accordingly, the difference in the degree of activation spreading between the noun and verb generation tasks (i.e. stronger for verbs than nouns) predicts the pattern of temporal cortex activation which we exactly found in our fMRI study, namely more activation for verbs than nouns.

Generally speaking our fMRI study fits well with our previous findings that both the selection between competing responses and association strength are important factors for single word production. Association strength, however, becomes critical only in the verb generation task and particularly when task-irrelevant responses interfere with word production.

Some methodological generalizations can be drawn from the different approaches which were used to investigate the neural and cognitive basis of noun and verb generation. In the first chapter (section 1.1) we have shown that findings from neuroimaging studies and findings from cognitive models have been related only in a few cases which are mainly represented by the application of fMRI to test models derived from cognitive architecture (see Stocco & Anderson, 2008 for an example; see also Henson et al., 2000 for an example of relation between fMRI and connectionist models). Moreover, we also discussed that the issue of relating findings from neuropsychology and brain imaging has been a controversial one (see section 1.1 in chapter 1; see also Page, 2006; Coltheart, 2004; 2006).

In chapters 5 and 6 we have shown that the development of a detailed cognitive model of task performance (i.e. the FRI model), which we have repeatedly tested using experimental data of different subject populations (i.e. young adults, older adults, and PD patients), has made possible to link the findings from this model with those from brain imaging. As already shown, a specific unexpected neuroimaging finding such as the increased activation in temporal cortex for verbs relative to nouns have been interpreted in the light of the findings obtained on the FRI model (i.e. differences between tasks in the degree of activation spreading). In a similar way, the effects of selection demands which were evident in the mid LIFG in our brain imaging study (i.e. more activation in the mid LIFG for high than low selection conditions) but much less evident from a behavioural point of view (i.e. similar RT between high and low selection conditions), were also explained in relation to the equations used in our computational model (see sections 5.3.1 in chapter 5; 6.5 in chapter 6). In this latter example, fMRI has served a function of “Surrogate Behavioural Marker” (Cappa, 2006; see also section 1.1 of chapter 1) in the evaluation of theories which proposed the LIFG as playing a role in the selection of responses in situations of high competition (e.g. Thompson-Schill et al., 1997). Indeed, more conventional techniques such as reaction times had failed to show differences in performance in young adults in the conditions with strong association but different selection demands. Nevertheless the fMRI finding of an effect of selection demands was in line with the same effect which was found both in accuracy and RT in the verb generation task for the PD patients (see chapter 4). Furthermore, the neuropsychological finding of a deficit for the PD patients in the weak association condition of verb generation, has also helped to interpret the fMRI finding of a BG activation specific for weak associated verb responses. Moreover, both these findings have contributed to the interpretation, suggested by the FRI model, that these structures are particularly important for the selection of task-relevant responses in situations in which task-irrelevant responses are activated by the stimuli.

The multi-disciplinary approach used in this project has also contributed to better specify the processes underlying the tasks of noun and verb generation. Thus, the three approaches used have provided cumulative evidence that both the factors of response selection and association strength are important for single word generation.

More generally, the operation of linking functional imaging and neuropsychology findings on cognitive processes through a well specified model of normal cognition (i.e. the FRI model) has contributed to learn more about the process of selection of task-relevant responses in a poorly understood cognitive domain such as that of the higher levels of the language production system (see Shallice, 2003).

7.2. Limits and suggestions for future research

Several questions for future research can be formulated to further investigate the selection of task-relevant responses as well as the other aspects addressed in this thesis. First, a behavioural paradigm similar to that described in the second part of chapter 2 could be used in order to investigate whether and to what extent the noun and verb generation tasks used in chapters 4, 5, and 6, are influenced by a concurrent distracting motor task. Normal adult subjects could be asked to generate nouns and verbs which differ in selection demands and association strength while simultaneously carrying out either a less demanding or a more demanding version of a distracting motor task. Based on results obtained on tasks of sentence completion (see section 2.8.2 in chapter 2) we predict that the more demanding version of the dual task would specifically influence (i.e. increase in RT) the weak association condition of verb generation. In fact, as shown in previous chapters, this condition requires more processing demands than the conditions with strong association of verb generation and, more generally, than all conditions of noun generation and thus should be particularly subject to dual task interference. Moreover, in a similar fashion to the stem completion task, the strong association conditions of both tasks should be less influenced by the motor task, given that in these conditions, task-relevant responses may be retrieved and selected in a more automatic way.

As regards patient OTM it would have been interesting to investigate his verbal output production at the level of discourse generation, possibly using tests of the kind used by Robinson et al. (2006) with the dynamic aphasic patient KAS. A careful examination of OTM’s ability to generate multiple connected messages, through a series of discourse level generation tests, could help to assess whether he also has the same kind of problems that Robinson et al. (2006) proposed for their patient KAS, namely deficits “in focusing attention an a specific message to be expressed and subsequent shifting of attention” (Robinson et al., 2006, p. 1357). This could also be helpful in assigning OTM’s dynamic aphasia to one of the two subtypes of Robinson et al. (2006) with more certainty.

Some questions can also be formulated on the neuropsychological study of noun and verb generation carried out on PD patients (chapters 4). For example, it would be interesting to study whether the factors of response selection and association strength influence both noun and verb generation performance also when verbs, rather than nouns, are given as stimuli cues. In a previous neuropsychological study, Péran et al. (2003) administered the tasks of noun and verb generation from both noun and verb stimuli to a population of PD patients. They obtained similar patterns of impaired performance for the *noun-verb* and *verb-verb* tasks and preserved performance for the *noun-noun* and *verb-noun* tasks. Measures of selection demand and association strength could be calculated on verb stimuli in a similar way to what we have done for noun cues and free association norms could also be collected on verb stimuli. If PD patients were impaired on the *noun-verb* and *verb-verb* but not on the *noun-noun* and *verb-noun* tasks, in the context of free association norms showing nouns rather than verbs as dominant response, a position in terms of defective retrieval and selection of task-relevant responses rather than impaired grammatical knowledge could be further supported for PD patients.

With regards to the computational models, a cognitive model similar to the FRI model could be developed in which the primary cue is a verb rather than a noun (see figure 5.4 in chapter 4). A simulation could be run to make the model reproduces the performance of a new sample of PD patients on the *verb-noun* and *verb-verb* generation tasks.

As far as the COGENT model is concerned, it would be important to extend it to other tasks such as, for instance, sentence generation from weakly and strongly associated word pairs. Our experimental findings have shown that OTM could produce sentences from word pairs which were strongly associated while having problems when words were weakly related. A model focused on this task would explicitly address the issue of how associative strength between stimulus and response and between different responses influences performance. The set of equations of the ACT-R declarative memory system could also be used in order to investigate response selection at a more detailed level in this kind of task.

Another interesting extension of the COGENT model would make it including other macroplanning and/or microplanning processes such as those that intervene when the information to be expressed is more complex than that required by the sentence completion task. A model of a discourse level generation test should deal with the needs to, for instance, satisfy many successive communicative goals, order the information for expression, and keep track of the current discourse. The microplanning compound system of our model (see figure 3.3 in chapter 3) could be expanded and studied while interacting with the macroplanning components in an agent model of the selection of task-relevant information at the higher levels of discourse generation.

A last question concern the fMRI study and the way in which association strength and selection demands were operationalized in our set of studies. It has been argued that such variables are likely to be correlated, that is conditions differing on one measure tend to differ also on the other (see Thompson-Schill & Botvinick, 2006 and Snyder & Munakata, in press). Recently, Snyder and Munakata (in press) addressed this issue proposing new measures based on latent semantic analyses (LSA) designed to unconfound these two effects. Using LSA association values, Snyder and Munakata also calculated a new measure of competition, namely “entropy” which reflects the competition between all alternative responses, rather than just the two most common responses (as in our current study). Snyder and Munakata’s LSA measures may help to eliminate the potential problem of using relative, proportion-based measures, as in our and in previous studies (Thompson-Schill et al., 1997; Martin & Cheng, 2006; Persson et al., 2004). LSA-based measures of association strength and competition could be useful in future fMRI experiments of verb/noun generation helping to clarify further the functional segregation of controlled retrieval and selection (Badre et al., 2005).

7.3. Conclusions

This project aimed to investigate the function of the prefrontal cortex and basal ganglia of selection of task-relevant responses. A detailed task-analysis was performed for different tasks, namely sentence completion, noun generation, and verb generation; and a variety of approaches (i.e. cognitive modelling, cognitive neuropsychology, and functional neuroimaging) was used to pursuit our aim at both the cognitive level and neural level of investigation. Results of various experiments support the hypothesis that both the basal ganglia and the prefrontal cortex are crucial for the human ability to selectively adapt behaviour to different situations.

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Appendix

1. COGENT Macroplanning model (chapter 3).

The updating activation function employed in the Interactive Activation Network (IAN) is reported below. The content of each rule-based processor is also given. Elements in both the shared and general knowledge systems are reported for the stimulus sentence *"the children were.."*.

Interactive Activation Network:

Updating Activations

The new activation for each node depends on the current activation and on the current input to that node on each processing cycles. The activation function employed in our model is the same of that used by Cooper and Shallice (2000) and is given by the following equation:

$$A_{t+1} = \overline{\vartheta}(P.\overline{\vartheta}^{-1}(A_t) + IN_t)$$

where P is persistence (see table 3.1), A_t is the activation of the node on cycle *t*, IN_t is the net input to the node, and $\overline{\vartheta}$ is the hyperbolic tangent function which is scaled such that:

$$\overline{\vartheta}(+\infty) = 1$$
$$\overline{\vartheta}(0) = A_{rest}$$
$$\overline{\vartheta}(-\infty) = 0$$

The updating function is bounded by 0 and 1 and tends to Rest activation with zero net input. With negative net input, nodes may be inhibited below the value of rest activation. According to Cooper and Shallice (2000), persistence is necessary in order to maintain smoothly varying activation profiles that, in the absence of P, would oscillate between extreme values.

Rule-based processor:

....

Box Name: *Beliefs Generation*

Rule 1
TRIGGER: request(complete, P)
IF: not request(complete, P) is in Beliefs
action_of_completion(requeste(complete), [Act])
THEN: add request(complete, P) to Beliefs
add [Act] to Beliefs

Rule 2
TRIGGER: del(requested(complete, P))
IF: request(complete, P) is in Beliefs
THEN: delete request(complete, P) from Beliefs

```
Rule 3
TRIGGER:      deal_with(feedback(F))
IF:           current_illocutionaryact(Speech_Act) is in Beliefs
THEN:         delete all feedback(_) from Beliefs
              add feedback(F) to Beliefs
              delete plan(Any) from Plan

Condition Definition:
              action_of_completion(requeste(complete), [intend(S, know(hearer, proposition))]):-
              rule([request(complete)], [_]) is in General Knowledge
              know(proposition(Q)) is in General Knowledge
              action_of_completion(requeste(complete), [intend(S, intend_to_do(hearer,
              proposition))]):-
              rule([request(complete)], [_]) is in General Knowledge
```

………………………………………………………………………

Box Name: *Perception*

```
Rule 1:
IF:           request(complete, P) is in The hearer:Working Memory
              not requested(complete, P) is in Shared Knowledge
THEN:         send request(complete, P) to Beliefs Generation
              add request(complete, P) to Shared Knowledge

Rule 2:
IF:           request(complete, P) is in Beliefs
              not request(complete, P) is in The hearer:Working Memory
THEN:         send del(requested(complete, P)) to Beliefs Generation


Rule 3:
IF:           feedback(F) is in The hearer:Prepare feed-back for subjects
              current_illocutionaryact(Speech_Act) is in Beliefs
THEN:         send deal_with(feedback(F)) to Beliefs Generation
```

………………………………………………………………………

Box Name: *Evaluation*

```
Rule 1
IF:           Candidate is in Candidate Speech_Acts
              evaluate(Candidate, Value)
THEN:         delete all evaluation(previous_cand, previous_act) from Evaluated Speech Acts
              add evaluation(Candidate, Value) to Evaluated Speech Acts

Rule 2:
IF:           not selected(Candidate) is in Evaluated Speech Acts
              evaluation(Candidate, Max) is in Evaluated Speech Acts
              not evaluation(Other_candidate, Act) is in Evaluated Speech Acts
              Act is greater than Max
THEN:         add selected(Candidate) to Evaluated Speech Acts
              delete all evaluation(_, _) from Evaluated Speech Acts


Rule 3:
IF:           evaluation(Candidate, Value) is in Evaluated Speech Acts
```

```
                not Candidate is in Candidate Speech_Acts
THEN:           delete evaluation(Candidate, _) from Evaluated Speech Acts

Rule 4
IF:             feedback(F) is in Beliefs
                current_illocutionaryact(Speech_Act) is in Beliefs
                selected(Temp_Speech_Act) is in Evaluated Speech Acts
                do(S, inform(H, P)) is in Candidate Speech_Acts
THEN:           add selected(do(S, inform(H, P))) to Evaluated Speech Acts


Condition Definition:
                evaluate(do(S, inform(H, P)), 1):-
                [intend(S, know(hearer, proposition))] is in Beliefs
                evaluate_through_GK(true)
                discourse_focus(Focus)
                evaluate(do(S, request(H, P)), 1):-
                [intend(S, intend_to_do(hearer, proposition))] is in Beliefs
                evaluate_through_GK(false)
                discourse_focus(Focus)
                evaluate(do(S, request(H, P)), 0):-
                [intend(S, intend_to_do(hearer, proposition))] is in Beliefs
                evaluate_through_GK(true)
                discourse_focus(Focus)
                evaluate(do(fre, inform(H, P)), -1):-
                [intend(S, know(hearer, proposition))] is in Beliefs
                evaluate_through_GK(false)
                discourse_focus(Focus)

Condition Definition:
                discourse_focus(Focus):-
                request(complete, P) is in Shared Knowledge

Condition Definition:
                evaluate_through_GK(true):-
                fact(past(Q)) is in General Knowledge
                about(Q, children)
                evaluate_through_GK(false):-
                not fact(past(Q)) is in General Knowledge
                about(Q, children)

 Condition Definition:
                about(Proposition, Topic):-
                Proposition is composed of List
                Topic is a member of List
```

……………………………………………………………………

Box Name: *Problem Solving*

```
Rule 1
IF:             complete(Communication, Generate_sentence) is in Communicative Goals
                Communication is a member of [inform, request]
THEN:           send push(communicate(Communication)) to Goal Stack
                add Communication to Current State
Rule 2
IF:             communicate(Communication) is in Goal Stack
```

```
                    not goal_encode_act_achieved
THEN:               send push(test_for_preconditions) to Goal Stack

Rule 3
IF:                 test_for_preconditions is in Goal Stack
                    exists Communication is in Current State
                    test_for_preconditions(Person_location)
THEN:               add Person_location to Current State
                    send push(choice_goal) to Goal Stack
                    send pop to Goal Stack

 Rule 4
 IF:                choice_goal is in Goal Stack
                    exists Communication is in Current State
                    exists Person_location is in Current State
                    choose_for_speech_act(Speech, Action)
 THEN:              send push(choose_Speech_act) to Goal Stack
                    send pop to Goal Stack

 Rule 5
 IF:                choose_Speech_act is in Goal Stack
                    exists Communication is in Current State
                    exists Person_location is in Current State
                    choose_for_speech_act(Speech, inform)
 THEN:              send push(got_inform_speech_act) to Goal Stack


 Rule 6
 IF:                choose_Speech_act is in Goal Stack
                    exists Communication is in Current State
                    exists Person_location is in Current State
                    choose_for_speech_act(Speech, request)
 THEN:              send push(got_request_speech_act) to Goal Stack

 Rule 7
 IF:                got_request_speech_act is in Goal Stack
                    illocutionary_act(Request)
                    effect_of_action_request(C, Effects)
 THEN:              add Effects to Current State
                    send pop to Goal Stack

 Rule 8
 IF:                got_inform_speech_act is in Goal Stack
                    illocutionary_act(Inform)
                    effect_of_action_inform(C, Effects)
 THEN:              add Effects to Current State
                    send pop to Goal Stack


 Rule 9
 IF:                choose_Speech_act is in Goal Stack
                    goal_encode_act_achieved
                    knowref(speaker(S)) is in Shared Knowledge
                    knowref(hearer(H)) is in Shared Knowledge
                    knowref(sentence(P)) is in Shared Knowledge
```

```
THEN:          add do(S, inform(H, P)) to Candidate Speech_Acts
               add do(S, request(H, P)) to Candidate Speech_Acts
               clear Current State
               send pop to Goal Stack

Condition Definition
               illocutionary_act(request_act):-
               effect_of_action_request(Conditions, Effects)

Condition Definition:
               illocutionary_act(inform_act):-
               effect_of_action_inform(Conditions, Effects)

Condition Definition:
               effect_of_action_inform(Conditions, do(S, inform(H, 'the children were'))):-
               rule([speaker(S), hearer(H), location(S, L), location(H, L), intend(S, know(H, P)),
               know(S, P)], [do(S, inform(H, P))]) is in Shared Knowledge
               knowref(speaker(S)) is in Shared Knowledge
               knowref(hearer(H)) is in Shared Knowledge
               knowref(sentence(P)) is in Shared Knowledge

Condition Definition:
                effect_of_action_request(Conditions, do(S, request(H, 'the children were'))):-
               rule([speaker(S), hearer(H), location(S, L), location(H, L), intend(S, intend_to_do(H,
               P)), know(S, know(H, P))], [do(S, request(H, P))]) is in Shared Knowledge
               knowref(speaker(S)) is in Shared Knowledge
               knowref(hearer(H)) is in Shared Knowledge
               knowref(sentence(P)) is in Shared Knowledge
Condition Definition
               choose_for_speech_act(Speech, inform):-
               [intend(S, know(hearer, proposition))] is in Beliefs
               rule(_, _) is in General Knowledge
               rule([_], [know(S, Q)]) is in General Knowledge
               choose_for_speech_act(Speech, request):-
               [intend(S, intend_to_do(hearer, proposition))] is in Beliefs
               rule(_, _) is in General Knowledge
               rule([_], [know(S, know(H, Q))]) is in General Knowledge

Condition Definition:
               goal_encode_act_achieved:-
               do(S, inform(H, P)) is in Current State
               do(S, request(H, P)) is in Current State

Condition Definition:
               test_for_preconditions(location(X)):-
               knowref(speaker(S)) is in Shared Knowledge
               knowref(hearer(H)) is in Shared Knowledge
               knowref(location(H, X)) is in Shared Knowledge
               knowref(location(S, X)) is in Shared Knowledge
```

....

Box Name: *Monitoring & Goal generation*

```
Rule 1
IF:            request(complete, P) is in Beliefs
```

```
                 not current_illocutionaryact(Speech_Act) is in Beliefs
                 speaker_knows_task(Generate_sentence)
                 rule(C, A) is in Shared Knowledge
                 precondition_satisfied(C)
THEN:            add complete(inform, Generate_sentence) to Communicative Goals

Rule 2
IF:              request(complete, P) is in Beliefs
                 not current_illocutionaryact(Speech_Act) is in Beliefs
                 speaker_knows_task(Generate_sentence)
                 rule(C, A) is in Shared Knowledge
                 precondition_satisfied(C)
 THEN:           add complete(request, Generate_sentence) to Communicative Goals

Rule 3
IF:              Generate_sentence is in Communicative Goals
                 not request(complete, P) is in Beliefs
THEN:            clear Communicative Goals

Rule 4
IF:              feedback(F) is in Beliefs
                 current_illocutionaryact(Speech_Act) is in Beliefs
THEN:            delete feedback(F) from Beliefs
                 delete current_illocutionaryact(Speech_Act) from Beliefs
                 delete all selected(Temp_Speech_Act) from Evaluated Speech Acts


 Condition Definition:
                 precondition_satisfied([]).
                 precondition_satisfied([H|T]):-
                 speaker_knows(H)
                 precondition_satisfied(T)

Condition Definition:
                 speaker_knows(Inform_known):-
                 [intend(S, intend_to_do(hearer, proposition))] is in Beliefs
                 [intend(S, know(hearer, proposition))] is in Beliefs
                 speaker_knows(Location):-
                 knowref(Location) is in Shared Knowledge
                 speaker_knows(Axiom):-
                 Axiom is in General Knowledge

Condition Definition:
                 speaker_knows_task(generate_sentence):-
                 know(S, intend(H, intend_to_do(S, Complete))) is in Shared Knowledge
```

....

Box Name: Beliefs Update

```
Rule 1
IF:              selected(Temp_Speech_Act) is in Evaluated Speech Acts
                 not current_temp_illocutionaryact(Speech_Current) is in Beliefs
THEN:            add current_temp_illocutionaryact(Temp_Speech_Act) to Beliefs
```

Rule 2
IF: plan(Speech_Act) is in Plan
not current_illocutionaryact(Speech_Current) is in Beliefs
THEN: add current_illocutionaryact(Speech_Act) to Beliefs
delete all current_temp_illocutionaryact(Temp_Speech_Act) from Beliefs

....

Box Name: Plan Construction

Rule 1
IF: True
THEN: send go to Plan Construction

Rule 2
TRIGGER: go
IF: True
THEN: send go to Plan Construction

Rule 3
IF: [H] is the list of all Speech_Act such that Candidate is in Evaluated Speech Acts
not plan(do(S, request(H, P))) is in Plan
knowref(speaker(S)) is in Shared Knowledge
knowref(hearer(H)) is in Shared Knowledge
selected(do(S, request(H, P))) is in Evaluated Speech Acts
propositional_completition(false, P, Q)
get_information_onP(Unknown, Question)
[intend(S, intend_to_do(hearer, proposition))] is in Beliefs
THEN: delete all plan(X) from Plan
add plan(Question) to Plan

Rule 4
IF: [H] is the list of all Speech_Act such that Candidate is in Evaluated Speech Acts
not plan(do(S, inform(H, P))) is in Plan
knowref(speaker(S)) is in Shared Knowledge
knowref(hearer(H)) is in Shared Knowledge
selected(do(S, inform(H, P))) is in Evaluated Speech Acts
propositional_completition(true, P, Q)
THEN: add Q to Conceptual Knowledge
send excite(Q, 0.200) to Conceptual Knowledge

Rule 5
IF: [H] is the list of all Speech_Act such that Candidate is in Evaluated Speech Acts
not plan(do(S, inform(H, P))) is in Plan
knowref(speaker(S)) is in Shared Knowledge
knowref(hearer(H)) is in Shared Knowledge
selected(do(S, inform(H, P))) is in Evaluated Speech Acts
node(Q, X) is in Conceptual Knowledge
X is greater than 0.800
[intend(S, know(hearer, proposition))] is in Beliefs
THEN: delete all plan(_) from Plan
add plan(do(S, inform(H, Q))) to Plan
send excite(Q, -10) to Conceptual Knowledge

Rule 6
IF: plan(do(S, inform(H, Q))) is in Plan
not selected(do(S, inform(H, P))) is in Evaluated Speech Acts
THEN: delete plan(do(S, inform(H, Q))) from Plan

Rule 7
IF: plan(do(S, question(H, P))) is in Plan
not selected(do(S, request(H, P))) is in Evaluated Speech Acts
THEN: delete plan(do(S, question(H, P))) from Plan

Condition Definition:
get_information_onP(not_know_P, do(S, question(past(hearer, 'the children were')))):-
rule([_], [do(S, question(H, P))]) is in General Knowledge

Condition Definition:
propositional_completitition(true, 'the children were', decl(past(Q))):-
fact(past(Q)) is in General Knowledge
about(Q, children)
propositional_completitition(false, 'the children were', decl(past(Q))):-
not fact(past(Q)) is in General Knowledge
about(Q, children)

Condition Definition:
about(Proposition, Topic):-
Proposition is composed of List
Topic is a member of List

....
Box Name: *General Knowledge*

Initial Knowledge:
Comment: Axioms from standard modal logics by Hintikka 1962

Element: All instances of propositional tautologies
axiom(true(P), true(P))

Element: Agent's knowledge closed under implication
axiom((know(S, P) , know(S, implies(P, Q))), know(S, Q))

Element: An agent only knows things that are true
axiom(know(S, P)) , true(P)

Element: Axiom of introspection
axiom(know(S, P)) , know(know(S, P))

Comment: Rule of inferences

Element: Modus Ponens
rule([implies(P, Q), true(P)], [true(Q)])

Element: Necessitation
rule([true(P)], [true(know(P))])

Elements for the sentence: “*The children were*”
Element:
fact(past(play(children, football)))

Element:
fact(past(watch(children, television)))

Element:
fact(past(running(children, park)))

Element:
fact(past(go(children, school)))

Element:
fact(past(swimming(children, sea)))

Element:
fact(past(swimming(swimmer, sea)))

Element:
rule([request(complete)], [intend(S, know(hearer, Q))])

Element:
rule([intend(S, know(H, Q))], [know(S, Q)])

Element:
rule([request(complete)], [intend(S, intend_to_do(hearer, Q))])

Element:
rule([intend(S, intend_to_do(H, Q))], [know(S, know(H, Q)), know(S, not_know(S, Q))])

Element:
know(hearer(H))

Element:
know(proposition(Q))

Element:
rule([know(S, not_know(S, Q))], [do(S, question(H, P))])

....
Box Name: *Shared Knowledge*

Initial Knowledge:
Element: axiomatization of the act of informing
rule([speaker(S), hearer(H), location(S, L), location(H, L), intend(S, know(H, P)), know(S, P)], [do(S, inform(H, P))])

Element: axiomatization of the act of request
rule([speaker(S), hearer(H), location(S, L), location(H, L), intend(S, intend_to_do(H, P)), know(S, know(H, P))], [do(S, request(H, P))])

Element:
knowref(speaker(S))

Element: knowref(hearer(H))

Element: Shared knowledge
human(S)

Element:
knowref(sentence('the children were'))

Element: Shared Knowledge
human(H)

Element: Shared knowledge
knowref(location(S, office))

Element: Shared knowledge
knowref(location(H, office))

Element: S knows the task
know(S, intend(H, intend_to_do(S, Complete)))

....

Box Name: *Microplanning*

Rule 1
IF: plan(do(_, inform(_, P))) is in Plan
THEN: add preverbal_message_completed(inform, P) to Formulator: Formulator Input

Rule 2
IF: plan(do(S, question(past(H, P)))) is in Plan
THEN: add preverbal_message_completed(question, P) to Formulator:Formulator Input

....

Box Name: *Formulator*

Rule 1
IF: preverbal_message_completed(inform, X) is in Formulator Input
THEN: add lexical_phon_forms_completed(inform, X) to Articulator:Articulator Input

Rule 2
IF: preverbal_message_completed(question, X) is in Formulator Input
THEN: add lexical_phon_forms_completed(question, X) to Articulator:Articulator Input

....

Box Name: *Articulator*

Rule 1
IF: lexical_phon_forms_completed(X, P) is in Articulator Input
THEN: add phrase_completed(X, P) to The hearer: Prepare feed-back for subjects

....
Box Name: *The hearer*

Rule 1
IF: request(complete, P) is in Working Memory
THEN: send request(complete, P) to Talk to the subject

Rule 2
IF: phrase_completed(X, P) is in Prepare feed-back for subjects
not feedback(F) is in Prepare feed-back for subjects
plan(do(S, inform(H, decl(Q)))) is in Subject:Plan
fact(Q) is in Subject:Shared Knowledge
THEN: send feedback(correct) to Talk to the subject
add feedback(correct) to Prepare feed-back for subjects
add feedback(correct) to Subject:Shared Knowledge
delete phrase_completed(X, P) from Prepare feed-back for subjects
send stop to 1Macroplanning (Normal) with feed-back and Network

Rule 3
IF: phrase_completed(X, P) is in Prepare feed-back for subjects
not feedback(F) is in Prepare feed-back for subjects
plan(do(S, inform(H, decl(Q)))) is in Subject:Plan
not fact(Q) is in Subject:Shared Knowledge
THEN: send feedback(wrong) to Talk to the subject
add feedback(wrong) to Prepare feed-back for subjects
add feedback(wrong) to Subject:Shared Knowledge
delete phrase_completed(X, P) from Prepare feed-back for subjects

Rule 4
IF: phrase_completed(X, P) is in Prepare feed-back for subjects
not feedback(F) is in Prepare feed-back for subjects
plan(do(S, question(past(H, P)))) is in Subject:Plan
THEN: send search_for_answer to Talk to the subject
delete phrase_completed(X, P) from Prepare feed-back for subjects

Rule 5
TRIGGER: search_for_answer
IF: Answer is in Working Memory
THEN: send Answer to Subject:Perception
send stop to 1Macroplanning (Normal) with feed-back and Network

Rule 6
TRIGGER: feedback(wrong)
IF: feedback(wrong) is in Prepare feed-back for subjects
THEN: delete feedback(wrong) from Prepare feed-back for subjects
....

2. The FRI computational model (chapter 5).

General parameters estimation

First, each noun stimulus of each experimental condition of the two tasks was directly connected to the two most strongly associated task-relevant responses, which were selected on the basis of two pilot tests (i.e. the first pilot test was used to select stimuli in the verb generation conditions, and the second pilot test was used to select stimuli in the noun generation conditions; see chapter 4), and to the first two responses produced in a free-association test (see chapter 4). The associative strength of the links between primary cue and response nodes (both task-relevant and free-association; see *Sj1i* in figure 5.4) was derived from experimental data (see equation 3 in section 5.3.1). As shown in chapter 5, for each response node we used the ratio of the frequency of the response to the number of subjects who judged noun-noun, noun-verb, or noun-free association stimuli. The raw associative strength measures (range 0.1-0.7; see table 4.3 in chapter 4 for the values of mean associative strength) were then properly scaled (i.e. multiplied by 10) to obtain values similar to that used in other ACT-R models (Anderson & Lebiere, 1998). In particular we referred to the Stroop model of Altman and Davidson (2001). In this model, associative activation spreading from cues ranged between 4 and 9.

Base-rate activations of the stimulus and response nodes were fixed using the frequency values of the words as they were reported in the "*Veli Dictionary of Frequency for Italian Spoken Language*" (see Chapter 4).

The secondary cues (noun / verb) were included in the network as distinct nodes (see figure 5.4 of chapter 5; see also Martin & Byrne, 2006 and figure 5.2 in chapter 5) and connected to the word nodes belonging to their respective category. As already shown and suggested by the associative strength equation (see equation 2 in section 5.3.1), the strength of the links between a secondary cue and its associated word nodes (i.e. *Sj2i*) is inversely proportional to the number of the links ("fan effect", see Danker et al., 2008). We have used the "*Veli Dictionary of Frequency for Italian Spoken Language*", to estimate the number of verbs (1640) and nouns (5740). The noun/verb ratio thus mirrors the real "fan" of activation spreading from secondary cues and implies that the associations between the secondary cue nodes and the word nodes are stronger for verbs than nouns (see equation 2 in section 5.3.1).

The *S* parameter, which is involved in equation 2 (see section 5.3.1 of chapter 5), expresses the maximum associative strength and was fixed at 10. The maximum value of associative strength between a stimulus and a response was 0.96 and was found when subjects were given a noun stimulus of the LS-SA condition of verb generation; this means that 44/46 subjects gave the same task-relevant response when given this stimulus. A raw value of 0.96 corresponds to the scaled value of 9.6 (see above) which we approximated to 10. A value of 10 for the S parameter caused similar values for *Sj2i* and *Sj1i* (see figure 5.4 and equations 2 and 3 in section 5.3.1).

The rest of parameters were chosen relying on values adopted in previous ACT-R research (e.g., Anderson et al., 2004; Anderson & Lebiere, 1998; Altman & Davidson, 2001) and through the identification of the best-fitting values for a set of the data, namely the accuracy data of young adults in the noun generation task. Thus the parameter *F* which is involved in the retrieval time equation (see equation 5 in section 5.3.1) was fixed at 2 while the *s* parameter of equation 4 in section 5.3.1 was fixed at 7. The *F* parameter determines the magnitude of the activation effects on latency in ACT-R while the *s* parameter indicates the noise in the declarative memory module of ACT-R. The values of, respectively, 2 and 7 guaranteed an appropriate fit of the selected set of data (i.e. young subjects' performance on noun generation) and similar values have been adopted in previous ACT-R models (see Anderson & Lebiere, 1998).

As explained in chapter 5, when a task-irrelevant response node is retrieved (e.g. a noun response node is retrieved during verb generation) and inhibition works, the FRI model begins a new retrieval attempt. This causes a reallocation of attention given that, in these situations, more attention is focused on the secondary cue (i.e. *Wj2* is increased) at the expense of the attention placed on the primary cue (i.e. *Wj1* is decreased). In the FRI model the parameter **delta-w** is responsible for this shift of attentional weight from one cue to another after a retrieval failure. Thus, during a second retrieval attempt, *Wj2* is increased of **delta-w** while *Wj1* is decreased of the same quantity. Following the Stroop model of Altman and Davidson (2001) we fixed at 3 the number of retrieval attempts in which the FRI model could produce a response. We fixed **delta-w** at the value of 0.15 since with this value the FRI model could produce a task-relevant response node most of the time after 3 retrieval attempts.